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REVIEW ARTICLE

Ultrasound-Guided Nerve Blocks with Corticosteroids: Clinical Efficacy, Safety, and Particulate Risk

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Abstract

Background Ultrasound-guided peripheral and sympathetic nerve blocks have gained increasing acceptance in the management of both acute and chronic pain. The adjunctive use of corticosteroids in these blocks aims to prolong analgesic duration and improve block efficacy, yet concerns remain about their adverse effects and optimal use.

Methods This narrative review examines the pharmacologic basis for corticosteroid use in nerve blocks, summarizes the clinical applications of corticosteroids in ultrasound-guided nerve and sympathetic blocks, and evaluates the spectrum of adverse events associated with their use.

Results Key topics addressed include the distinction between particulate and non-particulate steroids, evidence from recent practice guidelines on safety and efficacy, and the impact of ultrasound guidance on block outcomes and complication rates. Current evidence suggests that imaging guidance may enhance safety, but that the incremental benefit of corticosteroids over local anesthetic alone remains variable across indications.

Conclusion We identify major gaps in the literature, including the lack of large randomized trials comparing steroid versus non-steroid injectables in ultrasound-guided blocks, and limited long-term follow-up of neuromuscular and endocrine complications. We outline recommendations for clinical practice and propose directions for future research.

Keywords Adverse effects, Corticosteroid methanetriol mixture, Dexamethasone, Endoscopic ultrasound-guided, Nerve block, Steroids

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1 Introduction

Nerve blocks, a prevalent regional anesthetic technique, represent a fundamental component of perioperative anesthesia and postoperative analgesia.[1] The use of peripheral nerve blocks, such as quadratus lumborum block (QLB) and fascia iliaca compartment block (FICB), is necessary to limit the use of opioids and substitute them with safer and more effective alternatives, as they can minimize adverse effects like opioid dependence or opioid-induced hyperalgesia while providing effective analgesia for acetabular fracture surgery.[2]

Ultrasound-guided nerve blocks have become increasingly accepted in both acute and chronic pain management due to their advantages over traditional methods.[3-5] This technique offers portable, radiation-free, real-time imaging, enabling precise visualization of neural structures and surrounding tissues.[4,5] This precision enhances safety and efficacy by enabling accurate needle placement and observation of local anesthetic spread, thereby reducing complications and improving block success rates.[1,6] Applications range from managing acute pain in extremity trauma, where they can reduce opioid reliance,[3] to chronic pain conditions in the head, neck, and lower limbs.[4,7]

Adjuvant drugs are frequently added to local anesthetics in peripheral nerve blocks to prolong their duration of action and enhance their efficacy, thereby improving postoperative pain control and potentially reducing opioid consumption.[8-11] These adjuncts can also help to decrease the required dosage of local anesthetics, which may mitigate dose-dependent adverse effects.[8,12] Common classes of adjuvants include alpha-2 agonists (e.g., dexmedetomidine, clonidine), non-steroidal anti-inflammatory drugs (NSAIDs), opioids, N-methyl-D-aspartate (NMDA) receptor antagonists, and corticosteroids.[8,9,13] Evidence suggests that intrathecal opioids may reduce the incidence of postoperative delirium and opioid consumption in elderly patients.[14] While many adjuvants are used off-label, they play a crucial role in optimizing pain management strategies.[10,15]

Corticosteroids, particularly dexamethasone, are widely used as adjuvants in nerve blocks to prolong analgesia and improve block characteristics.[16-18] Their utility stems from their anti-inflammatory properties and potential regenerative effects observed in preclinical studies, though human evidence remains limited.[19,20]

When added to local anesthetics like ropivacaine or bupivacaine, dexamethasone has been shown to significantly extend the duration of sensory and motor blockade.[21-25] This effect has been observed in various blocks, including interscalene brachial plexus blocks and erector spinae plane blocks.[26,27]

The increased use of corticosteroids in ultrasound-guided nerve blocks stems from their ability to provide prolonged postoperative analgesia, reduce pain scores, and decrease opioid consumption.[26,28] Ultrasound guidance further enhances the appeal of corticosteroids by allowing for precise delivery to the target nerve, potentially maximizing their local effect while minimizing systemic exposure.[29] This combination contributes to improved patient satisfaction and facilitates enhanced recovery after surgery.[30] Studies have demonstrated that corticosteroids, such as dexamethasone, can significantly extend the duration of analgesia compared with local anesthetics alone, making them valuable for managing pain in conditions such as carpal tunnel syndrome, trigeminal neuralgia, and various peripheral neuropathies.[31,32]

Ultrasound-guided nerve blocks encompass a heterogeneous group of techniques that differ substantially in anatomical targets, procedural objectives, and clinical indications.[4,33] These include somatic peripheral nerve blocks, primarily used for perioperative analgesia;[34] sympathetic nerve blocks, employed in chronic pain and headache disorders;[35,36] and selected fascial plane blocks that target interfascial spread rather than discrete neural structures.[37] Importantly, the rationale for corticosteroid use varies across these techniques, ranging from prolongation of local anesthetic effects in acute postoperative settings[38,39] to modulation of neurogenic inflammation and ectopic neural discharge in chronic and neuropathic pain conditions.[40] Failure to distinguish between these techniques and indications may obscure clinically relevant differences in efficacy and safety, underscoring the need for an indication-specific evaluation.

Previous reviews have evaluated corticosteroids as adjuvants in peripheral nerve blocks or focused on perineural dexamethasone primarily in the context of postoperative analgesia, often without differentiating between acute and chronic pain indications or accounting for the procedural implications of ultrasound guidance.[10,17,41] Other reviews have examined steroid use in peripheral neuropathies or discussed the safety of particulate versus non-particulate steroids, largely based on evidence from neuraxial and transforaminal epidural injections, where anatomical and vascular risk profiles differ from those of peripheral nerve blocks.[19,42,43] Consequently, a procedure-specific and indication-based synthesis of corticosteroid use in ultrasound-guided peripheral nerve blocks remains lacking. This narrative review addresses this gap by integrating pharmacologic mechanisms, particular risk considerations, ultrasound-related safety modulation, and clinical efficacy across postoperative, chronic musculoskeletal, neuropathic, and headache-related nerve blocks, providing a

contextualized perspective not comprehensively covered in prior reviews.

2 Search Methods

This narrative review was conducted using a structured literature search strategy. Electronic searches were performed in PubMed, Scopus, and Google Scholar up to 2025 for relevant literature. Search terms were used alone or in combination and included "corticosteroid", "dexamethasone", "methylprednisolone", "particulate steroid", "non-particulate steroid", "ultrasound-guided nerve block", "peripheral nerve block", "regional anesthesia", "perineural injection", and "nerve block adjuvant." Peer-reviewed articles were considered, including randomized controlled trials, observational studies, systematic and narrative reviews, meta-analyses, and relevant preclinical mechanistic studies. As this was a narrative review, no formal risk-of-bias assessment or quantitative synthesis was performed.

3 Addressing Scientific Gaps or Controversies

Despite their widespread use, several scientific gaps and controversies surround the use of corticosteroids in nerve blocks. Concerns persist regarding their long-term safety, particularly potential neurotoxicity and effects on neural regeneration.[19,44] While some studies suggest that corticosteroids may offer pain relief and promote nerve regeneration in peripheral nerve pathologies, their clinical utilization remains limited, and further investigation into their mechanism of action is needed.[19] There is also a lack of large randomized trials comparing steroid versus non-steroid injectates in ultrasound-guided blocks, and limited long-term follow-up data on neuromuscular and endocrine complications.[45] For instance, while corticosteroids may provide short-term pain relief in genicular nerve blocks (GNB) for knee osteoarthritis, their incremental clinical benefit over local anesthetics alone is not always clear, raising questions about their appropriateness given potential adverse effects.[45] Furthermore, the role of corticosteroids in certain conditions, such as piriformis syndrome, remains unclear.[46] The distinction between particulate and non-particulate steroids and their respective safety profiles also warrants further research.[47]

4 Pharmacology of Corticosteroids in Nerve Blocks

Corticosteroids exhibit complex pharmacokinetics,[20] and local administration has been explored to target peripheral tissues;[20,48] however, systemic absorption still occurs, and evidence supporting reduced systemic risk or direct treatment of peripheral nerve injury remains limited.[49-51] While the specific details of lipid solubility, extensive hepatic metabolism, and high protein binding (primarily to albumin and corticosteroid-binding globulin) for individual corticosteroids like dexamethasone and methylprednisolone in the context of nerve blocks are not explicitly detailed in the provided articles, general principles of corticosteroid pharmacokinetics apply. For instance, aging can increase the volume of distribution for lipid-soluble drugs, thereby prolonging their elimination half-life.[52] Studies on methylprednisolone have shown sex differences in its clearance, likely attributable to sex-specific hepatic metabolism.[53]

Both dexamethasone and methylprednisolone are corticosteroids used in various medical contexts. Dexamethasone is recognized as a potent anti-nausea agent and an effective anti-inflammatory compound,[54,55] with its pharmacological effects primarily attributed to anti-inflammatory and immunomodulatory mechanisms,[56-58] including inhibition of prostaglandin synthesis[59] and modulation of gene transcription;[60,61] other proposed mechanisms remain incompletely understood.[62,63] Prophylactic intravenous (IV) dexamethasone (8 mg) significantly reduced the incidence and severity of post-extubation cough and sore throat in patients undergoing elective laminectomy under general anesthesia, offering a safe adjunct to mitigate airway irritation without notable systemic adverse effects.[64] While specific details on dexamethasone sodium phosphate (hydrophilic) and methylprednisolone acetate (lipophilic, depot formulation) in nerve blocks are not extensively covered, research has compared their efficacy in other conditions, such as immune thrombocytopenia.[65]

The biological half-lives of corticosteroids can vary, and their genomic effects, mediated by receptor-dependent changes in protein synthesis, can persist longer than their plasma half-lives. For example, methylprednisolone's effects on adrenal suppression and gene expression (such as glucocorticoid-induced leucine zipper [GILZ]) have been studied, revealing sustained pharmacodynamic effects.[53,66]

Perineural administration of dexamethasone often yields longer analgesia compared to IV routes, particularly when co-administered with epinephrine. When epinephrine is added, perineural dexamethasone significantly prolongs the duration of analgesia compared to IV administration (mean difference of 3.96 hours). Without epinephrine, the effects of perineural and IV dexamethasone on analgesic duration are equivalent.[67]

Dose-response modeling indicates that perineural dexamethasone prolongs analgesia in a dose-dependent manner. For instance, doses of perineural dexamethasone between 1 mg and 4 mg, combined with ropivacaine for interscalene brachial plexus block, showed a dose-dependent increase in analgesic duration.[68] A systematic review and network meta-analysis suggest that while IV dexamethasone can be as effective as perineural

dexamethasone in prolonging analgesic duration, it may require higher doses.[69]

While moderate evidence supports the superiority of perineural dexamethasone over IV dexamethasone in prolonging analgesia duration (e.g., a mean difference of 2.73 hours in lower limb blocks), this difference may not always be clinically relevant. The most common dose of dexamethasone in trials comparing IV and perineural routes was 8 mg.[70]

5 Differences Between Corticosteroid Types (Particulate vs. Non-Particulate)

Corticosteroids employed in regional anesthesia, including peripheral nerve blocks and epidural injections, as summarized in Table 1, are categorized as either particulate or non-particulate based on their physical characteristics, such as particle size and solubility.[71] This distinction is crucial because it affects efficacy, duration of action, and safety, particularly the risk of embolization or neurotoxicity from inadvertent intravascular injection.[71,72]

Table 1 Corticosteroid classification, physical characteristics, and safety implications in nerve blocks

Corticosteroid category	Drug examples	Physical form	Primary risk	Typical recommendation	references
Particulate	Methylprednisolone acetate, Triamcinolone acetonide, Betamethasone acetate	Suspension with large, insoluble particles; depot formulation	Arterial embolization, spinal cord, or cerebral infarction following inadvertent intravascular injection	Generally avoided, particularly in high-risk anatomical regions or transforaminal approaches	(129), (43), (78)
Non-particulate	Dexamethasone sodium phosphate	Water-soluble solution; no true particles	Lower embolic risk; potential systemic absorption	Preferred agent for ultrasound-guided peripheral nerve blocks	(78,79), (82), (87)
Conditionally non-particulate	Betamethasone sodium phosphate	Soluble, but may crystallize when mixed with certain local anesthetics	Crystal formation with ropivacaine or levobupivacaine, introducing particulate-like risk	Use with caution; compatibility should be verified	(73), (74)

Particulate Corticosteroids consist of suspensions with larger particles, which lead to slower dissolution and prolonged local effects. Examples include triamcinolone, methylprednisolone, and betamethasone acetate.[71]

Non-Particulate Corticosteroids are soluble solutions with minimal or no particles, resulting in rapid systemic absorption. Dexamethasone is a primary example of a non-particulate formulation.[71] While betamethasone sodium phosphate is non-particulate, it can form large crystals when mixed with certain local anesthetics, such as ropivacaine or levobupivacaine, potentially introducing particulate-like risks. Dexamethasone sodium phosphate can form small crystals with ropivacaine or levobupivacaine but generally does not form identifiable crystals with lidocaine.[73]

Particulate steroids offer a depot-like, sustained release due to their slow dissolution, which can prolong their anti-inflammatory effects at the injection site. In contrast, non-particulate steroids dissolve immediately, leading to a quicker onset but a shorter local duration and faster systemic uptake.[71] The process of filtering particulate corticosteroid suspensions, such as triamcinolone acetonide and methylprednisolone acetate, through common filters (e.g., 5-μm and 0.2-μm) can result in a complete loss of the corticosteroid from the solution and the formation of agglomerates, thereby affecting the drug's dosage. The choice of diluent also influences agglomerate formation.[74]

Particulate steroids may provide slightly superior short-term pain relief in lumbar transforaminal epidural steroid injections (TFESIs).[75,76] A meta-analysis reported a greater pooled mean maximum change in Visual Analog Scale (VAS) scores in the particulate group compared to the non-particulate group. However, the non-particulate group showed a larger proportion of patients achieving more than 50% pain relief.[76]

Non-particulate dexamethasone has demonstrated efficacy comparable to particulate steroids in lumbar TFESIs, with some studies suggesting non-inferiority or even superiority in pain relief and functional improvement over 2 months.[77,78]

A primary concern with particulate steroids is the risk of vascular embolization, which can lead to severe neurological complications such as spinal cord infarction, paraplegia, or stroke, particularly when administered via cervical or transforaminal approaches.[71,72,78,79] Neurological complications are more frequently associated with particulate corticosteroids delivered through transforaminal injections.[78] At the cervicothoracic level, the incidence rate of neurological complications is higher with particulate steroid injections compared to non-particulate ones. Injections using non-particulate steroids or no steroids have been found to be equally safe.[72] The U.S. Food and Drug Administration (FDA) issued a safety warning in 2014 regarding the risks of epidural corticosteroid injections, noting that, though rare, neurological complications were more often linked to particulate corticosteroids.[78,79] Some non-particulate corticosteroid formulations may contain neurotoxic preservatives.[78] Despite these risks, one study indicated that with meticulous and safe technique,

cervical transforaminal epidural steroid injections (CTFESI) using predominantly particulate steroids (triamcinolone acetonide) resulted in only minor, self-resolving complications.[80]

Current guidelines recommend avoiding particulate steroids and formulations containing potentially neurotoxic preservatives due to the risk of serious complications. Non-particulate steroids, such as dexamethasone, are generally preferred due to their lower complication rates.[81] The Multisociety Pain Workgroup has advised the use of non-particulate steroids to mitigate the risk of embolization associated with particulate corticosteroids.[82] Consensus opinions from multidisciplinary expert groups and national organizations have developed clinical considerations to enhance the safety of epidural steroid injections, advocating for the use of non-particulate steroids.[43] However, current practices still show variability in steroid and diluent choices, with some practitioners continuing to use particulate corticosteroids for TFESIs and ropivacaine, which can form crystals with dexamethasone, potentially creating a particulate-like injectate.[73,82]

6 Clinical Applications of Corticosteroids in Ultrasound-Guided Nerve Blocks

Corticosteroids are utilized in various ultrasound-guided nerve blocks for both acute postoperative pain and chronic pain conditions,[83] with studies evaluating their efficacy and duration of effect.[84-86] Ultrasound guidance enhances the precision and safety of these procedures by allowing visualization of nerves and the spread of injectate.[87]

The clinical role of corticosteroids in ultrasound-guided nerve blocks depends on both the type of block performed and the underlying pain indication.[88,89] For clarity, applications are discussed according to block technique and corresponding clinical context.

- **Postoperative somatic peripheral nerve blocks**

In somatic peripheral nerve blocks used for postoperative analgesia, such as brachial plexus, femoral, and sciatic nerve blocks, corticosteroids, most commonly dexamethasone, are used as adjuncts to local anesthetics to prolong the duration of sensory block and reduce rebound pain.[90-92] This efficacy has been predominantly evaluated in single-shot ultrasound-guided techniques.[92] Dexamethasone, when added to local anesthetics in supraclavicular brachial plexus blocks, has been shown to result in a significantly faster onset of sensory and motor block, a prolonged duration of both sensory and motor block, and better postoperative pain control with reduced analgesic consumption.[92] Perineural dexamethasone has also been found to significantly prolong the duration of analgesia for interscalene nerve blocks using ropivacaine or bupivacaine.[93] Furthermore, perineural dexamethasone can improve postoperative pain outcomes by prolonging analgesia and motor block duration, and reducing postoperative opioid consumption, without reports of persistent nerve injury.[94,95] It can also prevent bupivacaine-induced rebound hyperalgesia and axon degeneration in a mouse sciatic nerve block model.[91] The use of dexamethasone as an adjuvant has been shown to reduce the intensity of rebound pain and the proportion of severe pain cases in patients with combat-related limb injuries.[90]

- **Chronic musculoskeletal and neuropathic pain blocks**

In contrast to postoperative nerve blocks, ultrasound-guided peripheral nerve blocks for chronic musculoskeletal and neuropathic pain, such as genicular or ilioinguinal nerve blocks, aim primarily to attenuate neurogenic inflammation and peripheral sensitization. In these indications, corticosteroids are often administered for their anti-inflammatory properties, and clinical outcomes are typically measured in terms of pain relief duration.[96]

For chronic knee osteoarthritis, ultrasound-guided GNB combined with a local anesthetic and a corticosteroid can provide short-term pain relief, although the clinical benefit of corticosteroid administration compared with local anesthesia alone is not always clear.[45,88] Perineural steroid injections around ilioinguinal, iliohypogastric, and genitofemoral nerves have been shown to ameliorate chronic refractory neuropathic pain in the lower abdomen and groin in patients who have not responded to conventional medical management.[97] Locally applied corticosteroids have been found to inhibit transmission in C-fibers. They can suppress ectopic neural discharges from injured nerve fibers, suggesting a beneficial effect in neuropathic pain when applied close to the site of nerve injury.[96]

- **Sympathetic and headache-related nerve blocks**

Sympathetic nerve blocks and headache-related procedures, including stellate ganglion, greater occipital, and sphenopalatine ganglion (SPG) blocks, constitute a distinct category in which corticosteroids are used to modulate autonomic dysfunction and neurogenic inflammation.[4,98] These techniques differ fundamentally from somatic peripheral nerve blocks in both anatomical target and therapeutic intent.[4]

Greater occipital nerve (GON) blocks are effective for the acute and short-term preventive treatment of migraine and cluster headache.[99-101] While GON blocks with local anesthetics are recommended for chronic migraine prevention, the use of steroids in GON blocks received a weak recommendation against use compared to local anesthetic alone for this indication.[102] SPG blocks are also used for headache management, including migraines and cluster headaches.[101,103,104] Evidence supporting

corticosteroid use in these contexts remains more heterogeneous and indication-dependent.[102]

Table 2 summarizes commonly reported dosing strategies, observed benefits, and key limitations across a range of ultrasound-guided nerve blocks.

Table 2 Dosing, efficacy, and limitations of corticosteroids across ultrasound-guided nerve block types

Block type	Steroid (typical dose)	Route	Reported benefit	Key controversy or limitation	references
Brachial plexus (interscalene, supraclavicular)	Dexamethasone (4–8 mg)	Perineural or IV	Prolonged sensory and motor block; reduced opioid consumption	Clinical relevance of perineural vs IV superiority remains debated	(93), (94), (84)
Genicular nerve block (knee OA)	Dexamethasone or Methylprednisolone	Perineural	Short-term pain relief	No consistent long-term superiority over local anesthetic alone	(45), (86)
GON block	Corticosteroid ± local anesthetic	Perineural	Effective transitional therapy in cluster headache	Limited or no added benefit in migraine prevention	(123), (124), (102)
Ilioinguinal/iliohypogastric/genitofemoral blocks	Corticosteroid + local anesthetic	Perineural	Reduction of neurogenic inflammation and neuropathic pain	Lack of large RCTs and long-term outcome data	(96), (97)
Sympathetic blocks (stellate, SPG)	Corticosteroid + local anesthetic	Perineural	Modulation of autonomic dysfunction; short-term symptom relief	Evidence heterogeneous and indication-dependent	(98), (103)

7 Adverse Effects and Safety Concerns

Corticosteroids are frequently utilized as adjuvants in nerve blocks, and understanding their potential adverse effects and safety concerns is crucial.[45] The method of administration, particularly the use of imaging guidance, influences the mechanical safety profile of these procedures;[105] however, it does not eliminate pharmacological risks associated with corticosteroid exposure.[106]

- **Safety with Ultrasound Guidance**

When nerve blocks are performed under ultrasound guidance, serious adverse events are generally reported as rare.[107] Ultrasound guidance enhances precision, allowing for real-time visualization of anatomical structures and needle placement, which significantly reduces complications and improves the success rate of the block.[108,109] Studies on ultrasound-guided procedures, such as GNB for knee osteoarthritis, have reported no postprocedural adverse events in patients receiving corticosteroids combined with local anesthetic, although the potential adverse effects of corticosteroids are still acknowledged.[45] Similarly, some investigations into ultrasound-guided corticosteroid injections for conditions like carpal tunnel syndrome have found no adverse events in either steroid-only or combination therapy groups.[110] However, local side effects associated with corticosteroid injections have been noted in some instances; for example, in a study comparing 5% dextrose (D5W) and corticosteroid hydrodissection for meralgia paresthetica, six patients in the corticosteroid group reported an adverse effect, whereas none were observed in the D5W group.[111] Overall, ultrasound-guided nerve blocks, when performed by trained providers, are associated with a low rate of complications .[112]

- **Risks Without Ultrasound Guidance**

In contrast, nerve blocks performed without ultrasound guidance, often referred to as “blind” techniques, carry a higher risk of complications due to the lack of precise needle placement.[109,113] Historically, procedures like intra-articular corticosteroid injections were performed blindly based on anatomical landmarks.[88] However, the absence of real-time visualization can lead to an inappropriate block and increase the potential for severe complications, including organ puncture (such as bowel or liver injury).[109] The use of ultrasound guidance has been shown to reduce the incidence of pain events and adverse reactions in nerve block treatments compared to ordinary (less guided) methods.[108] This suggests that blind injections may lead to less accurate drug delivery, potentially increasing local adverse effects if the corticosteroid is injected into unintended tissues.

- **General Adverse Effects of Corticosteroids in Nerve Blocks**

Although administered locally, perineural corticosteroids are absorbed into the systemic circulation and can produce classic glucocorticoid-related adverse effects, including hypothalamic-pituitary-adrenal (HPA) axis suppression, hyperglycemia, and osteoporosis.[114,115]

Beyond the risks associated with the guidance method, corticosteroids themselves can lead to specific adverse effects. While not always extensively detailed across all studies, local adverse effects such as hypopigmentation, subcutaneous fat atrophy, and nerve injury have been reported with local corticosteroid injections.[19,107]

Among the systemic adverse effects, HPA axis suppression is a recognized concern, with studies showing significant decreases in serum cortisol levels post-injection that may

take weeks to return to baseline.[116] The risk of such systemic effects is influenced by the dose and frequency of injections.[117]

Neurological complications can also arise, particularly with particulate corticosteroids like methylprednisolone, which have been associated with embolic events leading to serious conditions such as spinal cord infarction, cerebellar and brainstem infarction, and cortical blindness. To mitigate these risks, soluble, non-particulate steroids such as dexamethasone are often recommended for epidural injections.[116]

Other potential systemic effects of corticosteroids, which may be relevant in the context of nerve blocks, include transient hyperglycemia (especially in diabetic patients), an increased risk of infection (including abscess formation), osteoporosis, avascular necrosis, and cardiovascular effects such as hypertension. While specific details linking these directly to nerve blocks with corticosteroids were not extensively detailed in the retrieved literature, corticosteroids are known to have systemic effects, and their impact can depend on the dose and duration of exposure.[117]

The specific adverse events directly attributable to the corticosteroid component, beyond general procedural risks, are not always thoroughly documented in the literature.[1,118-121]

8 Current Controversies and Knowledge Gaps

- **Necessity as Adjuvants and Efficacy in Cluster Headaches**

There is ongoing debate regarding the necessity of corticosteroids as adjuvants to local anesthetics in many peripheral nerve blocks. While some studies demonstrate that perineural dexamethasone can prolong analgesia in brachial plexus blocks,[39,94,122] concerns about potential neurotoxicity have led some to suggest that IV administration may be a safer alternative with comparable effects.[94,123,124] For migraine, some research indicates that occipital nerve blocks with corticosteroids and local anesthetics do not significantly reduce headache frequency compared to placebo.[125] However, for cluster headaches, GON blocks with local anesthetics and corticosteroids are considered an effective transitional therapy, providing short-term relief and reducing attack frequency, duration, and severity.[126-128]

- **Long-term Efficacy in Radicular Pain**

Debates persist regarding the long-term efficacy of epidural steroid injections for radicular pain. A 2025 review by the American Academy of Neurology, incorporating 90 randomized controlled trials, provides definitive evidence regarding their short-term benefits. Epidural steroid injections (ESIs) probably reduce pain (success rate difference -24.0%, number needed to treat (NNT) = 4) and disability (NNT = 6) in the short term (≤ 3 months). However, there is insufficient evidence that ESIs reduce long-term pain (≥ 6 months), the effect on long-term disability is uncertain, and ESIs do not reduce the need for surgery. The NNT of 4 for short-term pain relief indicates a modest treatment effect; approximately 75% of patients will not experience significant benefit from a single injection, which falls short of what many clinicians and patients might expect from an invasive procedure. Furthermore, the lack of sustained benefit beyond three months means that ESIs should not be viewed as curative.[129] A 2025 clinical review emphasizes that ESIs serve as "bridge therapy," providing temporary relief to facilitate participation in physical therapy or other rehabilitative interventions while the underlying condition resolves on its own.(42) As highlighted by recent guidelines, patient selection significantly influences outcomes, with better responses in single-level radiculopathy due to disc herniation compared to multilevel pathology or concomitant spinal stenosis.

- **Peripheral Neuropathies and Lack of Human Trials**

The limited clinical adoption of corticosteroids for peripheral neuropathies contrasts with promising anti-inflammatory and regenerative effects observed in animal models.[19,20] There is a recognized lack of robust human trials demonstrating superior outcomes over standard therapies, and the long-term risks and benefits remain inadequately studied.[19,130]

- **Dosing and Administration Routes for Perineural Dexamethasone**

Knowledge gaps remain regarding the optimal dosing and routes of administration for perineural dexamethasone in brachial plexus blocks. While studies show prolonged analgesia,[39,68,122,131] data on dose-response relationships are inconsistent, with some suggesting a ceiling effect at 4 mg[131] and others showing dose-dependent effects at lower doses.[68,132] Concerns regarding potential neurotoxicity, derived primarily from animal studies and in vitro models, continue to fuel debate regarding the relative safety of perineural versus IV dexamethasone administration, as definitive long-term human data are lacking.[123,124,133]

- **Lumbar Spinal Stenosis and Functional Improvement**

For chronic low back pain with lumbar spinal stenosis, meta-analyses indicate uncertainty about whether epidural steroids provide superior functional improvement compared to local anesthetics alone. A 2015 meta-analysis concluded that both epidural injections with steroids and those with local anesthetic alone provided significant pain relief and functional improvement, with no additional advantage conferred by the inclusion of steroids.[134] There is no clear consensus on the optimal injection frequency to avoid cumulative risks, although

studies often report average numbers of procedures over time.[135,136]

- **Occipital Nerve Blocks for Migraines**

Controversies in occipital nerve blocks for migraines include whether corticosteroids provide additional benefit beyond local anesthetics. Randomized trials suggest equivalent clinical outcomes between local anesthetics alone and local anesthetics with steroids for migraine prevention.[125] However, some practitioners advocate their use as transitional therapy for cluster headaches, where they have shown efficacy.[126-128]

- **Nerve Regeneration Post-Injury**

While preclinical evidence supports corticosteroids' role in reducing inflammation and potentially aiding myelination in nerve regeneration post-injury,[19] clinical translation remains a gap. The complex environment of spinal cord injury, including glial scarring and inhibitory molecules, poses significant challenges to regeneration.[137,138] Insufficient randomized trials assessing functional recovery in humans limit the clinical application of these findings.[19]

- **Multisociety Guidelines and Comparative Effectiveness Research**

Multisociety guidelines underscore the need for more comparative effectiveness research on imaging-guided versus landmark techniques in steroid nerve blocks to resolve debates on procedural safety and patient selection criteria.[1,5] While ultrasound guidance is increasingly used and can improve safety and efficacy by allowing real-time visualization,[3,5] landmark-based techniques are still considered feasible and safe in certain contexts.[139] The optimal guidance method and patient selection criteria continue to be areas of active research.

- **Limitations of Preclinical and Indirect Evidence**

Throughout this review, we have cited animal studies and evidence from related fields (e.g., neuraxial injections, ophthalmology) to support mechanistic discussions. However, it is critical to acknowledge that findings from preclinical models and non-nerve block contexts may not directly translate to human ultrasound-guided peripheral nerve blocks. A recent comprehensive review highlights this disconnect, demonstrating how robust preclinical evidence suggesting benefit from regional anesthesia failed to translate into clinical benefit in large randomized trials involving 4,770 patients. The authors emphasize that reductionist, mechanism-focused preclinical research often overestimates treatment effects, and both basic scientists and clinicians have underestimated the limitations of preclinical models.[140] Therefore, while animal studies provide valuable mechanistic insights, they require confirmation in well-designed human trials before clinical application. Readers should interpret such evidence with appropriate caution.

9 Clinical practice points

The rationale for corticosteroid use differs fundamentally between acute postoperative analgesia and chronic pain management.[20,141,142] In postoperative somatic nerve blocks (e.g., brachial plexus, femoral), perineural dexamethasone (typically 4–8 mg) is effective in prolonging analgesic duration and reducing opioid consumption.[39,94,143,144] In chronic musculoskeletal or neuropathic pain blocks (e.g., genicular, occipital), corticosteroids are used primarily for their anti-inflammatory effects;[20] however, their incremental long-term benefit over local anesthetic alone is less certain and should be evaluated on a case-by-case basis.[141,145]

To minimize the risk of particulate-related vascular complications, non-particulate steroids (e.g., dexamethasone) are preferred over particulate formulations (e.g., triamcinolone, methylprednisolone acetate) for peripheral nerve blocks, especially in anatomical regions with proximity to named arteries.[146,147] Intravascular injection of particulate steroids during nerve blocks has been identified as a potential cause of severe neurological complications due to embolization and occlusion of blood vessels.[147,148] Studies have shown that particulate steroids, such as methylprednisolone, can lead to neurological deficits when inadvertently injected into arteries, while non-particulate steroids like dexamethasone do not.[148] Dexamethasone is considered a non-particulate steroid, whereas methylprednisolone acetate and triamcinolone acetonide contain particles, some of which can be larger than red blood cells and tend to aggregate.[149,150] These characteristics of particulate steroids significantly increase the risk of embolic infarcts following intra-arterial injection.[150]

10. Future Directions

- **Nanotechnology and Drug Delivery Systems**

Research is advancing in the development of new delivery systems for therapeutic agents that could potentially be applied to corticosteroids to improve their efficacy, duration of action, and safety profile in nerve blocks. For instance, the co-delivery of liposomal bupivacaine with liposomal dexamethasone phosphate and liposomal dexmedetomidine has been shown to significantly prolong the duration of sciatic nerve block compared to liposomal bupivacaine alone or with a single liposomal adjuvant. This approach also decreased tissue inflammation without significant myotoxicity, whereas unencapsulated adjuvants led to systemic side effects.[151] Other innovative delivery systems include ropivacaine-loaded hydrogels, which have demonstrated prolonged sensory and motor blockade and reduced neurotoxicity in preclinical studies[152] Nano-based drug delivery systems, encompassing polymeric, lipid, metallic, inorganic non-metallic, and hybrid nanoparticles, are also being

developed for local anesthetics to achieve more efficient drug release, prolonged action, and reduced systemic toxicity, which could be extended to corticosteroids.[153] Furthermore, aptamer-based depot systems are emerging as a method for sustained release of small-molecule therapeutics, showing potential to prolong local anesthesia and reduce systemic toxicity.[154]

- **Sustained-Release Corticosteroid Formulations**

Sustained-release corticosteroid formulations, including liposomal and depot-based preparations, are being developed to prolong analgesic duration and reduce the need for repeated injections, particularly for chronic pain conditions where extended modulation of neurogenic inflammation is desired.[155]

Various approaches for sustained-release local anesthetics and corticosteroids have been explored, including liposomal formulations, lipid-based nanoparticles, thermo-responsive nanogels, microspheres, microcapsules, and polymeric matrices.[155] For instance, liposomal morphine has demonstrated prolonged analgesia and decreased systemic toxicity in mouse models due to sustained release from the liposomal depot.[156] Similarly, liposomal dexamethasone phosphate has shown persistent anti-inflammatory effects in a mouse model of collagen-induced arthritis, with reduced typical glucocorticoid side effects compared with the free drug.[157]

In the context of intra-articular delivery, poly lactic-co-glycolic acid (PLGA) sustained-release systems aim to extend joint residence time and reduce reinjection frequency. Clinical studies have shown prolonged symptom relief with extended-release corticosteroid depots, such as PLGA-triamcinolone injections, demonstrating approximately 50% pain reduction over 12 weeks with a single dose.[158] Extended-release corticosteroids may offer additional clinical benefits compared with standard-release corticosteroids for conditions such as knee osteoarthritis.[159]

However, challenges remain, including variability in release kinetics, limited peripheral nerve block-specific safety data, and concerns regarding prolonged tissue exposure. Further safety studies are required to ensure the safe and effective utilization of sustained-release local anesthetics, and the release kinetics of various formulations need to be adequately established.[155] The translation of these systems also hinges on manufacturing scale-up and quality systems that maintain critical particle attributes and enable informative in vitro–in vivo interpretation.[158]

- **Novel Adjuvant Combinations**

Combining corticosteroids with other agents is an active area of investigation. Corticosteroids are frequently administered with local anesthetics in nerve blocks.[160-162] While some studies indicate that combining corticosteroids with local anesthetics in GNB can provide short-term pain relief, the long-term clinical benefit compared to local anesthetic alone is not consistently clear, and potential adverse effects warrant careful consideration.[45] Oral corticosteroids as a premedication have also been shown to improve the anesthetic effect of nerve blocks and provide better analgesic efficacy compared to NSAIDs for postendodontic pain.[161] The use of platelet-rich plasma (PRP), either in conjunction with corticosteroids or as an alternative to them, is also being explored. For instance, in periarthritis of the shoulder joint, a suprascapular nerve block combined with PRP showed superior long-term outcomes compared to a steroid and suprascapular nerve block, although steroids provided better short-term results.[163] Other studies comparing PRP and corticosteroid injections for conditions like carpal tunnel syndrome and plantar fasciopathy have yielded mixed results, with PRP sometimes showing longer-term benefits while corticosteroids offer more immediate relief.[164-167] The use of other adjuvants, such as α2 agonists like dexmedetomidine, in liposomal formulations with corticosteroids and local anesthetics, has demonstrated enhanced efficacy in prolonging nerve blockade.[151]

11. Conclusion

Corticosteroids combined with local anesthetics in nerve blocks provide anti-inflammatory effects and effective short- to mid-term pain relief in specific conditions such as occipital neuralgia, postendodontic pain, and certain neuropathic pain states. They suppress C-fiber transmission and inhibit glial activation in neuropathic pain models. However, their efficacy varies considerably across indications, and long-term benefits beyond several months remain unproven. While preclinical studies have suggested potential regenerative effects, these findings have not been consistently replicated in human trials, and complete functional recovery following nerve injury is rarely achieved with corticosteroid therapy alone. Furthermore, as highlighted in recent multisociety guidelines, the addition of corticosteroids does not consistently improve outcomes compared to local anesthetics alone in several common procedures, such as sympathetic nerve blocks and migraine prophylaxis. Image-guided nerve blocks are associated with low reported complication rates; however, the true incidence remains uncertain, and injectate choice must prioritize mechanism, efficacy, and safety for the specific clinical condition. Risks include surgical site infection if timed poorly with surgery. Repeated patient education on expectations and full disclosure of risks and benefits are essential for informed consent, with corticosteroids applied judiciously due to limited evidence in peripheral neuropathies.

Significant gaps remain in mechanisms, optimal dosing, drug types, and patient selection. Long-term studies are critical to assess sustained effects and complications like infection or atrophy. Robust trials with extended follow-up are needed to optimize efficacy, minimize risks, and clarify roles in chronic pain management.

Declarations

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