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Review Article **Orthopedic Surgery**

Review Article on Safety of Epidural Steroid Injections for Lumbosacral Radicular Pain

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Abstract

***Background*:** Lumbosacral radicular pain, commonly known as sciatica, is a prevalent and challenging condition arising from nerve root compression in the lumbar spine due to various underlying pathologies. Epidural steroid injections (ESIs) are often employed for symptomatic relief when conservative treatments fail. While ESIs are minimally invasive and provide localized pain relief, their safety, especially concerning neurological complications, remains a critical concern. ***Objective*:** This article reviews the neurological complications associated with ESIs and compares the safety and effectiveness of various corticosteroid formulations administered via transforaminal, interlaminar, or caudal injection techniques. ***Method*:** A comprehensive literature search was conducted using PubMed, Scopus, and the Cochrane Library, focusing on studies published within the last ten years. Inclusion criteria encompassed studies addressing lumbosacral radicular pain, the safety and efficacy of ESIs with different corticosteroid formulations, and comparative effectiveness analyses of injection routes. Data on corticosteroid types, formulation characteristics, adverse effects, efficacy measures, and patient demographics were extracted and analyzed both qualitatively and quantitatively. ***Results*:** Findings indicate significant variation in safety profiles and effectiveness among different corticosteroid formulations used in ESIs. Dexamethasone, often favored for its efficacy, has been linked to potential neurological complications, particularly concerning preservatives like benzyl alcohol. Comparative studies suggest that while dexamethasone may provide adequate pain relief, it may lead to higher rates of repeat injections compared to particulate steroids like triamcinolone. ***Conclusion*:** The review underscores the need for a personalized approach to ESI administration, balancing the benefits of pain relief against potential long-term complications. The data highlights a pressing need for ongoing research into optimizing corticosteroid use and ensuring patient safety in the management of lumbosacral radicular pain.

Keywords: Lumbosacral radicular pain, sciatica, epidural steroid injections, corticosteroids.

INTRODUCTION

Lumbosacral radicular pain, often termed sciatica, is a common and challenging condition characterized by radiating pain from the lower back into the buttocks, legs, and sometimes the feet. This pain results from nerve root compression or irritation in the lumbar spine, typically due to conditions such as disc herniation, spinal stenosis, or degenerative spinal disorders. For patients with persistent symptoms who do not respond adequately to conservative treatments, epidural steroid injections (ESIs) are frequently recommended to provide targeted relief. By delivering corticosteroids directly to the epidural space near the affected nerve roots, ESIs aim to reduce inflammation and alleviate pain, potentially improving function and quality of life [1-4].

ESIs have gained popularity in pain management due to their minimally invasive nature and the immediate, localized effect they offer compared to systemic medication. However, their safety profile has been a topic of ongoing discussion among clinicians and researchers, particularly in terms of adverse effects, risks associated with repeated use, and specific concerns for certain populations. While many patients experience

significant pain relief and improved mobility following ESIs, there is a need for more comprehensive research on their long-term safety and efficacy [5-9].

Key safety concerns related to ESIs include potential complications associated with the corticosteroids themselves, such as hormone disruption, immune suppression, and blood sugar elevation in diabetic patients. Additionally, the injection procedure carries inherent risks, such as infection, bleeding, nerve injury, and, though rare, severe complications like dural puncture or spinal cord compression. While these risks are low, they are important considerations when recommending ESIs, particularly in patients with pre-existing health conditions [10-12].

Recent studies have also explored the potential for epidural steroid injections to contribute to adverse effects on bone health, including osteoporosis and increased fracture risk with repeated or high-dose injections [13, 14]. These risks, coupled with the rising incidence of corticosteroid resistance in some patients, underscore the need for a personalized approach when considering ESIs as a treatment option. Practitioners must weigh the benefits of pain relief against potential long-term complications, particularly in individuals requiring multiple injections over time.

Another aspect of ESI safety involves the technique used, with approaches such as transforaminal, interlaminar, and caudal injections offering varying degrees of accuracy, efficacy, and safety profiles. The choice of approach may affect the risk of specific complications and is often influenced by the location and severity of the patient's condition, as well as clinician expertise. While fluoroscopic or CT guidance has improved the accuracy of ESIs and minimized procedural risks, it is not universally employed, which may affect outcomes and complication rates.

Objective

This article aims to review the neurological complications associated with epidural steroid injections (ESIs) and to compare the formulations, safety, and effectiveness of commercially available corticosteroids administered via transforaminal, interlaminar, or caudal injection.

METHODOLOGY

Literature Search

A comprehensive literature search was conducted to identify studies addressing the neurological complications associated with epidural steroid injections (ESIs) and the safety and efficacy of various corticosteroid formulations. Databases including PubMed, Scopus, and Cochrane Library were utilized. The search terms included "lumbar radicular pain," "sciatica," "epidural steroid injections," "corticosteroids," "safety," "neurological complications," and "transforaminal injections." Only studies published in English within the last 10 years were included to ensure the relevance and currency of the data.

Inclusion Criteria

Studies were included if they met the following criteria:

- Focused on patients with lumbosacral radicular pain or sciatica.
- Reported on the safety and efficacy of ESIs using different corticosteroid formulations.
- Discussed neurological complications or adverse effects associated with ESIs.
- Included comparative effectiveness analyses of transforaminal, interlaminar, or caudal injection routes.

Data Extraction

Data were extracted from the identified studies, focusing on the following key variables:

- Types of corticosteroids used (e.g., dexamethasone, triamcinolone, betamethasone).
- Formulation characteristics (e.g., presence of preservatives, solubility).
- Safety profiles, including reported adverse effects and complications.
- Effectiveness measures, such as pain relief outcomes, duration of relief, and need for repeat injections.
- Patient demographics, including age, sex, and underlying health conditions.

Analysis

The extracted data were analyzed qualitatively and quantitatively. Efficacy was assessed through statistical measures such as pain score reductions (e.g., Visual Analog Scale) and functional outcome scores (e.g., Oswestry Disability Index). Safety was evaluated based on the incidence of complications, including neurological effects and other adverse events associated with ESIs.

Summary

This review aims to synthesize current evidence on the safety and effectiveness of various corticosteroids used in ESIs for treating lumbosacral radicular pain, with a focus on identifying any neurological complications associated with these treatments. The findings will inform clinical practice and guide future research on optimizing corticosteroid use in this patient population.

RESULTS

Table-1: Food and Drug Administration (FDA)-approved Injectable Corticosteroids [2]

Corticosteroid	Tradename(s) (Manufacturer)	Suspension/ Solution	Solubility	Notable Excipients	Approved Routes of Administration
Betamethasone acetate, betamethasone sodium phosphate	Celestone Soluspan (Merck Sharp & Dohme)	Suspension	Acetate insoluble; sodium phosphate soluble	Benzalkonium chloride (for multidose use)	Intramuscular Intra-articular Soft tissue Intralesional
Methylprednisolone acetate	Depo-Medrol (Pharmacia and Upjohn Co.)	Suspension	Insoluble	Benzyl alcohol Polyethylene glycol Polysorbate 80 (for multidose use) Or Polyethylene glycol Myristyl-gamma-picolinium-chloride (for single-dose use)	Intramuscular Intra-articular Soft tissue Intralesional
Triamncinolone acetonide	Kenalog-10 Kenalog-40 Kenalog-80 (Bristol Myers Squibb)	Suspension	Insoluble	Benzyl alcohol Polysorbate 80 (for multidose use)	Intra-articular Intralesional Intramuscular*
Methylprednisolone sodium succinate	Solu-Medrol (Pharmacia and Upjohn Co.)	Solution	Soluble	Benzyl alcohol (for multidose use) Or Preservative-free (for single-dose use)	Intravenous Intramuscular
Dexamethasone sodium phosphate	Decadron (Merck)	Solution	Freely soluble	Benzyl alcohol with or without sodium sulfite (for multidose use) Or Methylparaben Propylparaben Edetate disodium (for multidose use) Or Preservative-free (for single-dose use)	Intravenous Intramuscular (intra-articular, intralesional, soft tissu

Table-2: Preservatives in Corticosteroid Injections

Additive	Neurotoxic Effects
Polyethylene glycol	Direct injection into carotid arteries in rats caused hemorrhagic brain injury
	Reversible dose-related depression of compound action potentials of rabbit vagus nerves: 20%-30% caused, while 40% caused abolition of compound action potentials (concentrations above 40% not studied as it was too viscous)
Benzyl alcohol	Neurotoxic effects in rodents after oral administration
	Flaccid paraparesis in mother after postdelivery epidural injection containing 1.5% benzyl alcohol in a 0.9% saline solution
	Seizures were observed following injection of 4.5% benzyl alcohol and death occurred following injection of 9% benzyl alcohol in dogs. There is a single case report of paralysis following inadvertent subarachnoid injection of 40 mL of normal saline that contained 1.5% benzyl alcohol
EDTA	Convulsions in mice after spinal injection
Sodium sulfite	Irreversible paralysis after subarachnoid administration in rabbits
Benzalkonium chloride	Arachnoid fibrosis after intrathecal injection in sheep
Myristyl-gamma-picolinium chloride	Toxicity in rat dorsal root ganglia sensory neurons

Table-3: Comparative-effectiveness of Dexamethasone Versus Particulate Steroids in the Treatment of Lumbar Radiculopathy with Interlaminar Epidural Steroid Injection and Caudal Injection Technique

Study Type	Dexamethasone Dose (mg)	Comparator Dose	Patient Exposure	Results
Randomized, controlled trial comparing dexamethasone and triamcinolone in patients with lumbar disc herniation	7.5	40 mg triamcinolone	106	VAS pain score reduction: triamcinolone 4.1±1.9 vs. dexamethasone 2.4±0.9 No significant difference in functional outcomes at 1 mo
Retrospective comparative-effectiveness outcomes study of dexamethasone vs. triamcinolone or betamethasone in patients with lumbar radicular pain	10	80 mg triamcinolone or 12 mg betamethasone	2634	52.4% of dexamethasone patients had ≥50% pain reduction at 2 mo vs. 44.2% of particulate steroid group
Randomized, double-blind comparative-effectiveness study of dexamethasone vs. triamcinolone in patients with intervertebral disc herniation	10	40 mg triamcinolone	78	Trend favoring triamcinolone at 2-wk follow-up that was not observed at 3 or 6 mo Dexamethasone patients had more repeat injections (17%) than triamcinolone patients (3%) (*P*=0.005)
Randomized, double-blind controlled trial comparing the effectiveness of dexamethasone and betamethasone for lumbosacral radicular pain	7.5	6.0 mg betamethasone	56	No differences in VAS pain and ODI scores between the 2 groups at 3 mo. At 6 mo, improvement in ODI score marginally favored dexamethasone (*P*=0.050)
Retrospective comparative-effectiveness study in patients with lumbar radicular pain	15	12 mg betamethasone 80 mg triamcinolone	78	No statistical difference in success rate between particulate steroids (35%) and nonparticulate steroids (28%) at short-term follow-up (<30 d; *P*=0.50) or intermediate follow-up, or the proportion who required repeat injections (27% vs. 39%)
Retrospective comparative-effectiveness outcomes study of particulate vs. nonparticulate corticosteroids in patients with lumbar radicular pain	4	40 mg triamcinolone acetonide	494	Higher proportion of patients treated with particulate steroids were improved at 1 wk (43.2% vs. 27.7%, *P*=0.001) and at 1 mo (44.3% vs. 33.1%, *P*=0.019) Patients receiving particulate steroids also had significantly higher NRS change scores at 1 wk (*P*=0.02) and 1 mo (*P*=0.007)
Retrospective comparative-effectiveness outcomes study of dexamethasone vs. triamcinolone in patients with lumbar radiculopathy	4	40 mg triamcinolone acetonide	418	Overall chance of pain reduction ≥50% was lower for dexamethasone-treated patients than triamncinolone-treated patients 4 wk postlumbar ESI (OR=0.55; *P*<0.012) Superiority of triamcinolone was dependent on baseline pain level, as low levels of baseline pain resulted in similar proportion of patients achieving ≥50% pain reduction

DISCUSSION

Several safety and comparative-effectiveness studies suggest dexamethasone as the preferred first-line medication for transforaminal epidural steroid injections (TFESI). However, the Benelux group within the World Institute of Pain (WIP) did not endorse a nonparticulate steroid as the primary choice for these injections. While dexamethasone is widely recommended, safer alternatives are still needed. Available dexamethasone formulations vary, with some containing benzyl alcohol,

a preservative with neurotoxic effects at high concentrations. Additionally, studies indicate that pain relief from epidural dexamethasone may be shorter-lasting than from particulate steroids. In a recent retrospective study of 94 patients receiving TFESI with dexamethasone for lumbosacral radicular pain, one-third reported no meaningful relief; some experienced no improvement (9.6%), while others had pain return to baseline within 3 days (23.4%) [15]. None achieved complete relief 2 weeks post-injection, and all required a second injection. Frequent injections may increase safety risks due to cumulative steroid exposure and the procedural risks involved.

CONCLUSION

Epidural steroid injections (ESIs) are among the most frequently utilized interventional treatments for lumbosacral radiculopathy, demonstrating the ability to alleviate pain and enhance function in appropriately selected patients, often for extended periods. They are a vital component of a multimodal treatment approach for managing lumbar and cervical radicular pain and are generally considered to carry fewer risks than surgical alternatives. While evidence is mixed, some studies indicate that ESIs may help reduce short-term opioid usage. Although no corticosteroids have received FDA approval specifically for epidural injection, extensive research over the past 50 years has established their efficacy and safety, leading to widespread application in treating lumbosacral radiculopathy.

Overall, complication rates from ESIs are low, with the most common issues being vasovagal reactions, increased radicular pain, and localized pain at the injection site. Systemic side effects, such as elevated blood glucose levels, can occur. Serious temporary or permanent neurological complications are rare and typically associated with the use of particulate corticosteroids administered via the transforaminal route. While a direct causal relationship has only been confirmed in animal studies, numerous case reports suggest an increased risk with transforaminal particulate steroids.

Multiple randomized trials and a meta-analysis have demonstrated that transforaminal epidural steroid injections (TFESIs) offer greater pain relief and functional improvement compared to interlaminar epidural steroid injections (ILESIs) for unilateral radicular pain. Consequently, most clinical guidelines advocate for the use of nonparticulate steroids like dexamethasone as the preferred first-line treatment for TFESI due to their improved safety profile and comparable effectiveness. The safety of dexamethasone formulations may be enhanced by using preservative-free, sterile options, although this needs to be weighed against potential reductions in efficacy or duration of effect. Therefore, developing new formulations with increased residency time at the injection site could provide an ideal balance to enhance both safety and effectiveness.

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