Epidural Steroid Injections: Are They Still Useful?

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7.1 Background

Low back pain is one of the leading causes of disability and health care expenditure [1], with escalating prevalence in the United States and globally [2].

Epidural injection with corticosteroids is a common treatment option for patients with lower back pain and sciatica.

Jean Sicard and Fernand Cathelin performed the first epidural injections around 1900 in Paris, injecting small volumes of local anesthetics into the sacral hiatus. The first recorded use of epidural steroid injections dates back to 1952, when Robecchi and Capra reported the relief of lumbar and sciatic pain after a periradicular injection of hydrocortisone onto the first sacral roots through the S1 posterior sacral foramen [3].

Over the past several decades, the technique and indications for epidural injections have changed substantially. A variety of anesthetics as well as a number of glucocorticoids (hydrocortisone, methylprednisolone, triamcinolone, dexamethasone) have been used. The caudal approach, originally described by Sicard and

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Cathelin, has largely been replaced by interlaminar and transforaminal injections that are typically performed with fluoroscopic guidance [4].

Since the 1970s, numerous clinical trials evaluated the effectiveness of epidural corticosteroid injections. Even though, epidural injections are one of the most commonly performed procedures in managing low back and radicular pain, conflicting recommendations have been provided, despite the extensive literature.

7.2 Anatomy

The spinal epidural space is located between the fusion of the spinal and periosteal layers of dura mater at the foramen magnum, superiorly and the sacrococcygeal membrane, inferiorly. The posterior longitudinal ligament, vertebral bodies, and discs lie anteriorly and the ligamentum flavum, capsule of facet joints, and laminae lie posteriorly. The pedicles and intervertebral foraminae lie laterally.

The epidural space contains fat, the dural sac, spinal nerves, blood vessels, and connective tissue [5].

7.3 Approach

Epidural injections are administered by accessing the lumbar epidural space by multiple routes—caudal, transforaminal, and interlaminar.

The interlaminar epidural steroid injection (ILESI) approach is considered to deliver the medication close to the assumed site of pathology, and a parasagittal, paramedian, or midline approach is used through the space between the lamina of the vertebrae. The needle first penetrates the skin, then subcutaneous tissue, paraspinal muscles, (the interspinous ligament—in the case of the midline approach), and then finally the ligamentum flavum. The "loss of resistance" technique is used to verify penetration into the dorsal epidural space and to avoid advancing the needle to far anteriorly and puncturing the dura mater [6].

The transforaminal epidural steroid injection (TFESI) approach is considered a target-specific modality requiring the smallest volume to reach the primary site of pathology. The procedure involves administering steroids under fluoroscopic guidance into the intervertebral foramen that lodges the affected spinal nerve. With an oblique needle approach, the most common target area is the posterior surface of the vertebral body, adjacent to the caudal border of the pedicle above the target nerve, commonly described as a subpedicular approach [7]. Two alternative approaches for TFESI include the retroneural approach and the retrodiscal approach.

The caudal epidural steroid injection (CESI) approach is considered the safest and perhaps the easiest, with minimal risk of inadvertent dural puncture and, therefore, of inadvertent intrathecal injection. CESIs do require relatively high volumes. The needle is introduced into the epidural space via the sacral hiatus. The needle will pass through the skin, subcutaneous fat, and sacrococcygeal ligament (SCL).

7.4 Patients' Selection: Indication

The most common indications for ESI are: radicular pain related to herniated nucleus pulposus, followed by neurogenic claudication or radiculopathy from lumbar spinal stenosis, and to a much lesser extent discogenic pain [8].

7.5 Rationale for the Use of ESI

Radicular pain occurs as a result of both mechanical nerve compression and a chemoinflammatory response. Mechanical compression, such as that from herniated disc material or foraminal osteophytes, can cause local structural changes to nerve roots leading to demyelination, axonal transport block, vascular changes, intraneural edema, and stimulation of an inflammatory reaction [9].

One can have classic radicular pain even without neural impingement seen on imaging modalities. This is attributable to the chemoinflammatory response that is best understood as a result of herniated nucleus pulposus. An annular tear exposes the highly antigenic nucleus pulposus, triggering an inflammatory cascade that contributes to localized neural edema, altered nerve function, and sensitization. In essence, the body responds to the herniated disc material as a foreign body [9].

Given the chemoinflammatory contribution to pain, corticosteroids provide a rational treatment approach. Corticosteroids decrease inflammation through inhibition of prostaglandins in the arachidonic acid cascade, which may improve microcirculation through decreasing capillary permeability, nerve root edema, and ischemia [10].

7.6 Risk

Complications from LESI are rare and can be classified according to the generic risks of all types of injections in general, those due the pharmacologic effects of steroids and local anesthetic agents, and those pertaining to the epidural site of injection.

Procedural complications include infection, hematoma, intravascular injection, dural puncture, air embolism, vasovagal syncope, intra-arterial injection of particulate steroid, neural puncture, and allergic reaction.

Severe infection is exceedingly rare, with a reported incidence of 0.01–0.1% for all spinal injections. Most often the result of needle introduction of skin flora with inadequate sterile technique during the procedure or the preparation of the injectate, reported infections include meningitis, epidural abscess, vertebral osteomyelitis, and discitis [11]. A large number of devastating fungal infections in the United States were caused by steroid preparations that were produced in a facility with grossly inadequate quality control processes, and the outbreak affected more than 700 patients, some have died, others had major complications, and some suffered

chronic sequelae [12]. The primary pathogen was *Exserohilum rostratum*, a plant pathogen that rarely causes human disease. To keep the risk of infection low, ESIs should not be performed when a patient has a concurrent bacterial infection such as a urinary tract infection and cellulitis. In such cases, the injection should be deferred until antibiotics have been completed for several days, and the patient has no signs of ongoing infection.

Epidural hematomas are rare in patients with normal clotting factors, with an overall incidence reported to be 1 in 150,000 epidurals [11], and an unknown proportion developing neurologic injury. Careful screening of patients to identify prescribed anticoagulant medications, clotting disorders, etc., will help to reduce the risk of epidural hematomas.

Vasovagal syncope is a risk with any type of injection, and it occurs in up to 1–2% of LESI patients. Symptoms are usually self-limited with removal of the needle and supportive care.

The incidence of headache is about 1% following lumbar injections. Its mechanism has not been established. It may be due to unrecognized dural puncture with resultant leakage of cerebrospinal fluid or inadvertent injection of air into the subarachnoid space.

The incidence of dural puncture ranges from 0.16% to 1.3% [13]. Inadvertent dural puncture does not constitute a complication in its own right, if it is recognized. The major risk of dural puncture is that, if it goes unrecognized, drugs will be delivered into the intrathecal space. If so injected, local anesthetics may cause spinal anesthesia, and steroid preparations may have neurotoxic effects because of the additives that they contain [14]. The risk of a "high spinal" is far greater during cervical epidural steroid injections, and we recommend using preservative-free corticosteroid and sterile saline with no local anesthetic in the epidural injectate for cervical ESIs.

Intravascular uptake occurs at a rate of 8% for all lumbar injections, and theoretical effects of intravascular anesthetic may include dizziness, tinnitus, nausea, muscle twitching, metallic taste, cardiac arrhythmia, seizures, or coma.

More feared but rare complication is spinal cord injury. There have been very few case reports of this complication in patients who underwent lumbar transforaminal injections [15, 16]. The mechanism of injury has not been explicitly demonstrated, but the prevailing view is that the injection penetrates a radicular artery and that when particulate steroids are injected they act as an embolus and infarct the conus medullaris.

For this reason, investigators have studied the prevalence and size of particles in various steroid preparations. Results have differed with respect to average size of particles and the size of aggregates that they form, but as a general rule, preparations of methylprednisolone and triamcinolone tend to have large particles capable of embolizing a small artery, preparations of betamethasone may or may not have particles, and dexamethasone exhibits no particles [17]. We use non-particulate steroid (dexamethasone) for all transforaminal epidural steroid injections.

Nerve damage also is a theoretical risk with nerve puncture and associated intraneural hematoma formation. Any solution injected into a nerve could potentially be

neurotoxic, but this complication is unlikely to occur in an awake patient who will report paresthesias and pain, if the needle tip even grazes the nerve. Advancing the needle very slowly, when it might be in proximity to the nerve, is advisable.

Complications related to the solutions injected are rare. Hypersensitivity or anaphylactic reactions most often occur with contrast, but occasionally to anesthetic or its preservative. Consultation with an allergist may be beneficial when a patient's history of prior reactions raises the concern of a possible reaction during an ESI. In the case of ILESIs, where there is a concern for a possible contrast allergy, we will typically just perform the injection without contrast.

Corticosteroids often cause well-described side effects with systemic therapy, and these can occur to a lesser extent with ESI. Important considerations include elevation of blood sugars in diabetics with an average increase of 106 mg/dl on the evening of the injection and significant increased levels for 3 days [18]. This concern is heightened in patients with a history of brittle diabetes, and consultation with an internist or endocrinologist for recommendations about insulin sliding scales and other measures will reduce the risk of ESIs in such patients. Some fluid retention can occur, and thus caution is taken in patients with congestive heart failure. Case reports also exist of ESI causing Cushingoid syndrome and temporary adrenal suppression, but evidence has not yet linked ESI directly to bone loss or osteonecrosis [11]. Iatrogenic cushing's syndrome has been described in patients who underwent ESIs while taking highly active anti-retroviral therapy [19].

7.7 Efficacy

Epidural corticosteroid injections are most commonly performed for radiculopathy due to a herniated disc, but may also be given for spinal stenosis and to a lesser extent axial pain.

Evaluation of the efficacy of ESIs is challenging. Many limitations hinder the comparison of studies: variability in the methods used to select patients for inclusion, the variability of treatment protocols and patient selection, lack of appropriate or uniform outcome measures, and lack of fluoroscopy in many studies.

Given the heterogeneity of primary research, review articles and guidelines understandably arrive at mixed conclusions.

7.8 Axial Lower Back Pain

Sayegh et al. [20]. Compared blind caudal ESI to caudal injection of lidocaine, in patients with LBP for more than 1 month, with or without sciatica, and MRI evidence of HNP or disc degeneration. They found significant improvement in Oswestry Disability Index in both groups over time up to 1 year, with earlier improvement in disability and straight-leg raise tolerance in the steroid group.

Southem et al. [21]. A retrospective study evaluated 84 patients with axial LBP refractory to conservative treatment at 3 months and MRI evidence of disc

pathology at L4–5 or L5–S1, without stenosis, who received a fluoroscopically guided caudal ESI. At an average follow-up of 28 months after the injection, only 23% met strict criteria for successful outcome.

7.9 Spinal Stenosis

Botwin et al. [22]. A prospective cohort study evaluated 34 patients with unilateral radicular pain from degenerative lumbar spinal stenosis who did not respond to conservative management and subsequently underwent fluoroscopically guided lumbar transforaminal epidural injections. Patients were followed up to 12 months after the injection. Seventy five percent of the patient had successful long-term outcome, reporting at least a >50% reduction between preinjection and postinjection pain scores, with an average of 1.9 injections per patient. Sixty-four percentage of patients had improved walking tolerance, and 57% had improved standing tolerance at 12 months. This study had no control group.

Friedly et al. [23]. In a multicenter, double-blind trial, 400 patients who had lumbar central spinal stenosis and moderate-to-severe leg pain and disability were randomly assigned to receive epidural injections of glucocorticoids plus lidocaine or lidocaine alone. The patients received one or two injections before the primary outcome evaluation, performed 6 weeks after randomization and the first injection. The primary outcomes were the score on the Roland–Morris Disability Questionnaire (RMDQ) and the rating of the intensity of leg pain. At 6 weeks, there were no significant differences in the RMDQ score or the intensity of leg pain between the two groups. Both groups, lidocaine only and lidocaine with glucocorticoids, improved in the study, raising the possibility that both arms of the trial had a therapeutic effect perhaps by flushing out inflammatory mediators from the epidural space.

7.10 Sciatic Pain

7.10.1 IESI

Dilke et al. [24]. One hundred patients with unilateral sciatic pain due to lumbar disc disease were randomly assigned to the treatment group (epidural injection of 80 mg of methylprednisolone) or the control group (superficial injection of normal saline into the interspinous ligament). Outcome analysis found statistically significant differences only in certain secondary outcome measures, such as return to work at 30 days. With respect to relief of pain, epidural injection of steroids was not demonstrably more effective than injection of normal saline into an interspinous ligament. All the procedures were done by the same physician using non-image-guided technique. One study found that even when the procedure was performed by an experienced anesthesiologist, 25% of the injections were not epidural [25].

Ridely et al. [26]. Double-blind study of 39 patients with sciatic pain, who receive either an epidural injection of 80 mg methylprednisolone or an interspinous

injection of normal saline. The results showed that epidural injection of steroids achieved greater improvements in pain than did an injection of saline into an interspinous ligament. Baseline data and final outcomes, however, were not reported, and the effects attenuated after 12 weeks.

Carette et al. [27]. In a randomized, double-blind trial, comparing the epidural injections of methylprednisolone acetate (80 mg in 8 ml of isotonic saline) or isotonic saline (1 ml) to 158 patients with sciatica due to a herniated nucleus pulposus. Patients were evaluated at 3 weeks, 3 months, and 12 months. The study concluded that epidural injections of methylprednisolone may afford short-term improvement in leg pain and sensory deficits in patients with sciatica due to a herniated nucleus pulposus, but this treatment offers no significant functional benefit nor does it reduce the need for surgery.

Valat et al. [28]. In a randomized, double blind, controlled clinical trial, patients with sciatica were assigned to receive three epidural injections (2 day intervals) of either 2 ml prednisolone acetate (50 mg) or 2 ml isotonic saline. Forty two patients were included in the control group and 43 patients in the steroid group. The study found no statistically significant difference in outcome. Although a slightly larger proportion of patients were relieved by steroids at day 20 after treatment, the difference was not significant. By day 35, the proportions relieved were essentially identical.

Price et al. [29]. A prospective, multicenter, double blind, randomized, placebo-controlled trial with 12-month follow-up was performed. Total of 228 patients clinically diagnosed unilateral sciatica, aged between 18 and 70 years, who had a duration of symptoms between 4 weeks and 18 months. Patients received up to three injections of epidural steroid and local anesthetic (active), or an injection of normal saline into the interspinous ligament (placebo). ESI led to a transient benefit in Oswestry Disability Questionnaire (ODQ) and pain relief, compared with placebo at 3 weeks There was no benefit over placebo between weeks 6 and 52 (1 year).

7.10.2 TFESI

Weiner et al. [30]. The only strong evidence that transforaminal injections spare patients from surgery. An observational study that used a novel outcome measure. That study enrolled 30 patients with severe lumbar radiculopathy secondary to foraminal and extraforaminal disc herniation who were on a waiting list for surgery. After being treated with transforaminal injections of steroids, 47% obtained complete relief of pain that was lasting and only 20% required surgery. The efficacy of transforaminal injections was cast in terms of their ability to spare patients from having surgery.

Lutz et al. [31]. A prospective observational study reported that 52 out of 69 patients obtained greater than 50% relief of the pain after treatment with transforaminal injections of steroids at follow-up times of between 28 and 144 weeks.

Riew et al. [32]. A prospective, randomized, controlled, double-blind study. Used avoidance of surgery as the outcome measure. Fifty five patients who were referred to surgery because of lumbar radicular were prospectively randomized into the

study. They then were randomized and referred to a selective nerve root injection with either bupivacaine alone or bupivacaine with betamethasone. It found that only 8 of 28 patients (29%) required surgery after treatment with transforaminal injections of betamethasone, compared with 18 out of 27 patients (67%) treated with transforaminal injections of bupivacaine. The difference in the operative rates between the two groups was highly significant ($p < 0.004$). A later publication [33] reported a 5-year follow-up of these patients, which showed that the majority of patients with lumbar radicular pain who avoid an operation for at least one year after receiving a nerve root injection with bupivacaine alone or in combination with betamethasone will continue to avoid operative intervention for a minimum of five years. In neither publication were pain scores or disability reported.

Ng et al. [34]. A randomized, double-blind controlled trial. Eighty-six patients with radicular pain who had unilateral symptoms and who failed conservative management were recruited. The patients were randomized to receive either transforaminal injection of methylprednisolone and bupivacaine with or transforaminal injections of bupivacaine alone. The study found no differences at 1 day, 4 weeks, 6 weeks, or 3 months. In the two groups, pain scores dropped from 73 to 54 and from 77 to 55, respectively.

Thomas et al. [35]. Controlled trial compared transforaminal injections of steroids with conventional interlaminar injections. No differences in outcome were evident at 6 days after treatment, but by 30 days and at 6 months after treatment, those patients treated with transforaminal injections showed statistically significant greater improvements in pain and function relating to work and leisure. Small sample of 31 patients.

Ghahreman et al. [36]. In a prospective, randomized study, of 150 patients, compared the outcomes of transforaminal injection of steroid and local anesthetic, local anesthetic alone or normal saline, and intramuscular injection of steroid or normal saline. A significantly greater proportion of patients treated with transforaminal injection of steroid (54%) achieved relief of pain than did patients treated with transforaminal injection of local anesthetic (7%) or transforaminal injection of saline (19%), intramuscular steroids (21%), or intramuscular saline (13%). Although the relief of pain was correlated by improvements in function and disability, and reductions in use of other health care, the magnitudes of improvements in desired activities were not significantly different between treatment groups. Over time, the number of patients who maintained relief diminished. Only some maintained relief beyond 12 months.

7.10.3 Meta-Analysis

Pinto et al. [37]. Epidural Corticosteroid Injections in the Management of Sciatica: A Systematic Review and Meta-analysis.

Twenty three trials were included. The pooled results showed a significant, although small, effect of epidural corticosteroid injections compared with placebo for leg pain in the short term (mean difference, −6.2 [95% CI, −9.4 to −3.0]) and

also for disability in the short term (mean difference, −3.1 [CI, −5.0 to −1.2]). The long-term pooled effects were smaller and not statistically significant.

Cho et al. [38]. Epidural Corticosteroid Injections for Radiculopathy and Spinal Stenosis. A Systematic Review and Meta-analysis.

Thirty placebo-controlled trials evaluated epidural corticosteroid injections for radiculopathy, and 8 trials were done for spinal stenosis. For radiculopathy, epidural corticosteroids were associated with greater immediate-term reduction in pain (weighted mean difference on a scale of 0 to 100, −7.55 [95% CI, −11.4 to −3.74]), function (standardized mean difference after exclusion of an outlier trial, −0.33 [CI, −0.56 to −0.09]), and short-term surgery risk (relative risk, 0.62 [CI, 0.41–0.92]). Effects were below predefined minimum clinically important difference thresholds, and there were no longer term benefits. Limited evidence showed no clear effects of technical factors, patient characteristics, or comparator interventions on estimates. There were no clear effects of epidural corticosteroid injections for spinal stenosis.

Critique of this study pointed that Cho et al. utilized a novel theory converting active-controlled trials into placebo-controlled trials to prove their hypothesis that epidural steroids do not provide significant benefit.

Manchikanti et al. [39]. Epidural Injections for Lumbar Radiculopathy and Spinal Stenosis: A Comparative Systematic Review and Meta-Analysis.

Thirty nine randomized controlled trials met inclusion criteria. There were nine placebo-controlled trials evaluating epidural corticosteroid injections, either with sodium chloride solution or bupivacaine, compared to placebo injections. There were 12 studies comparing local anesthetic alone to local anesthetic with steroid.

A comparison of lidocaine to lidocaine with steroids in seven studies showed significant effectiveness from baseline to long-term follow-up periods.

Meta-analysis showed a similar effectiveness for pain and function without non-inferiority of lidocaine compared to lidocaine with steroid at 3 and 12 months.

7.11 Conclusion

Epidural steroid injections have been performed for many decades and are generally considered a very safe and moderately effective treatment for back and leg pain. When performed by an experienced physician using fluoroscopic guidance, the risk of experiencing a serious complication is rare. Overall, ESIs are usually well tolerated and represent a much less invasive option than surgery.

Clinical experience has taught us that ESIs are best used as a part of a multidisciplinary plan; injections are commonly coupled with other treatments (medications, physical therapy, etc.) in an attempt to either maximize the benefit or prolong the effects. Because disc herniations have a favorable history, providing temporary relief to a patient with an ESI may buy time to allow his or her body to resorb the extruded fragment. In some scenarios, this temporary relief may allow a given patient to avoid surgery.

As mentioned earlier, the evaluation of the efficacy of ESI is challenging. Majority of the studies are limited by the small sample size and the inherit difficulty in

randomization in interventional procedures. Different studies have different variabilities in patient selection, treatment techniques, outcome measures, and analysis methods. Which make comparison and meta-analysis of these studies difficult to interpret and utilize. Also there is ongoing controversy regarding the choice of steroid.

The current data suggests that ESI is best used for radicular symptoms with the goal of pain management in the acute to subacute setting to help patients be more comfortable as they progress through the generally favorable natural history of spontaneous improvement. The transforaminal route, which has been studied most recently, appears to be the most efficacious approach for monoradicular symptoms, secondary to a disc protrusion. Further placebo-controlled studies are necessary to define more conclusively the role of ESI for the various causes of radicular pain and to define the best technique for each indication.

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