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Evidence-informed management of chronic low back pain with epidural steroid injections

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Abstract **EDITORS' PREFACE:** The management of chronic low back pain (CLBP) has proven very challenging in North America, as evidenced by its mounting socioeconomic burden. Choosing amongst available nonsurgical therapies can be overwhelming for many stakeholders, including patients, health providers, policy makers, and third-party payers. Although all parties share a common goal and wish to use limited health-care resources to support interventions most likely to result in clinically meaningful improvements, there is often uncertainty about the most appropriate intervention for a particular patient. To help understand and evaluate the various commonly used nonsurgical approaches to chronic low back pain, the North American Spine Society has sponsored this special focus issue of *The Spine Journal*, titled Evidence-Informed Management of Chronic Low Back Pain Without Surgery. Articles in this special focus issue were contributed by leading spine practitioners and researchers, who were invited to summarize the best available evidence for a particular intervention and encouraged to make this information accessible to nonexperts. Each of the articles contains five sections (description, theory, evidence of efficacy, harms, and summary) with common subheadings to facilitate comparison across the 24 different interventions profiled in this special focus issue, blending narrative and systematic review methodology as deemed appropriate by the authors. It is hoped that articles in this special focus issue will be informative and aid in decision making for the many stakeholders evaluating nonsurgical interventions for CLBP.

Keywords: Low back pain; Lumbar pain; Corticosteroids; Epidural steroid injection; Therapeutic agents

Description

History

Conventional medicine has commonly upheld the notion that 80% to 90% of low back pain (LBP) cases are because of an unknown etiology. This belief is mostly based on the early work of Dillane et al. who could not detect an identifiable cause of LBP in 79% of males and 89% of females in a general clinical practice [1,2]. Similar findings were presented by Nachemson, who estimated that only 15% of LBP had a demonstrable pathoanatomical explanation [3]. Valkenburg and Haanen reported objective evidence of disc prolapse in only 2% of patients with LBP, whereas 6% had objective findings of lumbago [4]. Lumbosacral spine abnormalities discovered by myelography [5], computed tomography (CT) [6], and magnetic resonance imaging (MRI) [7] are frequently observed in asymptomatic individuals; their prevalence increases with advancing age [7]. Furthermore, physical examination has been deemed unreliable to diagnose lumbar discogenic pain [8] or lumbar

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z-joint–mediated pain [9], and requires great skill and vast experience in detecting sacroiliac joint (SIJ)–related pain [10]. It should be noted that Dillane et al. performed their studies before the advent of advanced diagnostic modalities.

Studies using fluoroscopically guided, diagnostic spinal procedures have attempted to differentiate the various sources of LBP and reported that 39% (95% confidence interval 30%–50%) of LBP is because of internal disc disruption syndrome [8], 13% to 19% can be attributed to SIJ dysfunction [11,12], and 15% to 17% are related to painful z-joint(s) [13]. Their results suggest that 67% to 75% of LBP cases can be accurately diagnosed as discogenic-, sacroiliac-, or z-joint–mediated pain, a stark contrast to earlier findings [1–4].

Treatment options for chronic LBP (CLBP) should address the pathophysiology of the injured structure. Evidence suggests an increased production of proinflammatory mediators and cytokines because of disc herniation [14–19] and higher levels of interleukin (IL)-6, IL-8, and prostaglandin E2 (PGE2) in degenerative, nonherniated painful discs [20,21]. Cyclical mechanical loading of the disc coupled with inflammatory stimuli have increased PGE2 production by nuclear and annular disc cells in vitro, with a stronger reactivity in the latter models [22]. Painful degenerative lumbar intervertebral discs have higher concentrations of sensory fibers—located in the end plate and nucleus—than nonpainful discs [23,24], whereas both IL-8 and PGE2 induce hyperalgesia [25]. The combination of the abundant innervation of the disc and increased production of proinflammatory mediators suggests that discogenic pain may involve hyperalgesia [20].

Injection of corticosteroids into the anterior epidural space has long been used to bathe the posterolateral periphery of the annulus with discogenic CLBP to help curtail the biochemical stimulation of the intervertebral disc. The main goals of this approach are to improve pain and function and allow the patient to participate in a comprehensive physical therapy program addressing biomechanical deficiencies after this reduction of hyperalgesia. Before using epidural steroid injections (ESIs), the target disc must be confirmed as the source of pain. To ensure the success of this approach, the appropriate therapeutic medication deposited into the anterior epidural space must also gain access to sensitized nerve endings.

Subtypes

Three routes may be used to introduce therapeutic agents into the lumbosacral epidural space: caudal ESI (CESI), interlaminar ESI (ILESI) (also termed translaminar ESI), and transforaminal ESI (TFESI). The CESI approach was first described in 1901 by a French radiologist who injected diluted solutions of cocaine through the sacral hiatus to treat intractable LBP or sciatica [26]. It was not until 1957 that Cappio investigated the therapeutic benefit of injecting corticosteroid into the epidural space via the caudal approach [27]. The interlaminar technique was first described by Pages in Spain in 1921 [28], and therapeutic benefits of lumbar ILESIs were reported 40 years later [29,30]. The first report of a lumbosacral TFESI appeared in the Italian literature by Robechhi and Capra [31] who used this approach to successfully treat lumbar and sciatic pain. The CESI and ILESI are the most commonly used techniques, and can be performed without fluoroscopy, though there is a substantial likelihood of needle misplacement when using a so-called blind approach. If the needle is misplaced, the therapeutic agent will likely not reach the anterior epidural space, regardless of operator's clinical experience [32].

General description

CESI is performed by placing a spinal needle into the sacral epidural space by way of the sacral hiatus. Relative ease of performance in thin individuals without requiring fluoroscopy is the main advantage of this ESI approach. The sacral epidural space must be filled before the injected medication reaches the lumbar region, requiring large volumes which necessarily dilute the steroid mixture. Consequently, CESIs rarely reach the ventral epidural space or move higher than the L5–S1 segmental level [33]. In addition, personal experience has demonstrated that during the caudal instillation of medicine there is considerable discomfort, which is not perceived with the other routes of ESI administration. The ILESI approach offers the potential advantage of delivering medication directly into the lumbar region, hence closer to the putatively painful structure, but it is technically more demanding than CESI. The injected agent is deposited into the posterior epidural space without a guarantee that it will flow anteriorly [34]. Traditionally, these procedures have been performed by practitioners skilled in using surface landmarks for needle placement. The addition of fluoroscopy and contrast enhancement allowed the documentation of whether or not the medication reached the potential pain generator, maximizing the chance of therapeutic benefit. ILESIs achieve ventral epidural contrast spread in just 36% of attempts [34]. In contrast, TFESIs achieve ventral flow in 100% of injections [35]. Furthermore, vascular evacuation of the therapeutic medication occurs in 11% of CESIs and TFESIs, and in 2% of ILESIs [36,37], thus preventing the therapeutic agent from reaching its target. The instillation of therapeutic doses of corticosteroid into the anterior epidural space to maximally reach the targeted intervertebral disc is best accomplished by TFESIs rather than with ILESIs or CESIs.

Fluoroscopically guided percutaneous procedures to treat painful lumbar z-joints or SIJs target the joints directly with intra-articular steroid injection [38] or radiofrequency ablation [39]; these procedures are discussed in detail elsewhere in this supplement. Whereas TFESIs often place medication around the posterolateral perimeter of the

affected disc, CESIs and ILESIs often fail to do so and are consequently considered non–target specific ESIs.

Practitioner, setting, and availability

These interventions should be performed by a physician trained in the safe and competent administration of these procedures, and in life support training to address potential complications. TFESIs are best learned during a rigorous, comprehensive 1-year interventional pain or spine fellowship. Weekend cadaver workshops may also be useful during residency before deciding to pursue additional fellowship training. CESI and ILESI have traditionally been taught with hands-on workshops. All ESIs should be performed in a setting with ready access to intravenous fluids, cardiac and pulse oximetry monitoring, and code cart, such as a private practice, ambulatory surgery center, or hospital-based surgery center. ILESIs and CESIs can be performed without fluoroscopic guidance and require fewer staff and support personnel. However, TFESIs require specialized equipment typically available only in specialized surgical centers or hospitals. Although ultrasonography has been used in preclinical trials, further investigation is mandatory to examine ultrasonography's capacity to detect intravascular uptake [40,41].

Reimbursement

Pertinent current procedural terminology (CPT) codes include 62311(Injection, single [not via indwelling catheter], not including neurolytic substances, with or without contrast [for either localization or epidurography], of diagnostic or therapeutic substance(s) [including anesthetic, antispasmodic, opioid, steroid, and other solutions], epidural or subarachnoid; lumbar, sacral [caudal]), and 64484 (Injection, anesthetic agent and/or steroid, transforaminal epidural; lumbar or sacral, each additional level (List, separately in addition to code for primary procedure) for lumbar TFESIs and each additional level, respectively); 77003 is the current code for fluoroscopic guidance for needle placement (eg, biopsy, aspiration, injection, and localization device). Associated costs for each injection are approximately $275 for supplies and $2,850 in a hospital-based ambulatory surgery center using fluoroscopic control. Private insurers typically cover lumbar ESIs if a thorough system evaluation is completed including: 1) history of pain complaint including description, location, quality, severity, duration/timing, context, and modifying factors; 2) physical examination of associated signs and symptoms; 3) conservative therapy (physical/chiropractic therapy, oral analgesics/adjuncts, and activity modification) fails or is not feasible; and 4) adequate documentation of patient's response to therapy.

If these criteria are met, ESIs are deemed medically necessary if pain symptoms are radicular. There is a corroborative structural abnormality on imaging; physical examination reveals hypesthesia, hyporeflexia, or myotomal weakness, positive electromyogram which corresponds to the pain symptoms, or there are signs of dural tension on physical examination. Repeat ESIs should be performed no sooner than 7 days after a prior injection, and a second and third injection should only be performed if there is documented improvement with the previous ones.

Theory

Mechanism of action

The instillation of corticosteroid and anesthetic into the anterior epidural space introduces therapeutic agents with potent anti-inflammatory properties adjacent to suspected painful intervertebral discs. Local anesthetics help curtail inflammation by inhibiting phagocytosis, decreasing phagocytic oxygen consumption, reducing polymorphonuclear leukocyte lysosomal enzyme release, and diminishing superoxide anion production [42–46]. Additionally, anesthetics improve neural blood flow and dysfunction [47,48]. Corticosteroids are well known for their anti-inflammatory properties [49], and also stabilize neural membranes, suppress ectopic neural discharges [50], and may have direct anesthetic effect on small unmyelinated nociceptive C-fibers [51,52]. Painful lumbar intervertebral discs are innervated by substance-P containing nerve fibers [23,53], unmyelinated C-fibers, and thinly myelinated A delta fibers [24] that provide a substrate on which corticosteroids and local anesthetics exert therapeutic benefit. The nucleus pulposus of the lumbar intervertebral disc is biologically active, responds to proinflammatory cytokines most sensitively after degeneration [54], and once painful produces further proinflammatory mediators [20]. Hence, corticosteroids and local anesthetics may exert a therapeutic benefit by bathing the posterolateral annular fibers, which are most prone to injury [55–57], in solutions with anti-inflammatory and neural stabilizing effects.

Diagnostic testing required

Plain film radiography is required before ESI; MRI or CT can be used to further define suspicious abnormalities detected by plain films, or if suggested by the clinical presentation. MRI may help guide the spine specialist target the appropriate disc(s) level(s). Loss of disc height and decreased T2-weighted signal may be predictive of outer annular tears [58]. Similarly, high intensity zone lesions, marked by a localized peripheral area of increased T2-weighted signal, may indicate symptomatic annular disruption [58–60]. Provocative discography remains controversial, but has been used to reveal painful annular defects. Extension of dye into the outer annulus or beyond, and not the severity of disc degeneration, has demonstrated to be a strong predictor of concordant pain on discography [61]. An appropriate diagnostic evaluation of persistent

lumbar pain would include plain films to assess alignment, disc height, and stability. Persistent symptoms (greater than 6 months) recalcitrant to exhaustive conservative treatment measures warrant lumbar provocative discography to better delineate the segmental level of pain generation and whether or not a corroborative outer annular tear exists accounting for persistent lumbar pain. Findings of concordantly painful outer annular disruption on discography would suggest where to target TFESIs to maximally affect the patient's symptomatology. However, such a strategy has not been critically evaluated.

Indications and contraindications

The primary indication for ESIs is radicular CLBP. Despite minimal work having been completed investigating the efficacy of these interventions solely for axial lumbar spine pain [62], such injections are also routinely offered to patients presenting with nonradicular CLBP. However, the role of these injections to treat CLBP has not been well defined and is currently supported largely by conjecture and logic. Deciding which level to inject is influenced by imaging findings and pain referral zones, but is more commonly determined by initially targeting the levels most likely to be responsible for discogenic CLBP (L4–5 and L5–S1) [8,61]. If the patient experiences only short-term or no improvement with a S1 TFESI, lumbar discography would be warranted to determine if one or both of the lowest two discs, or perhaps an upper level disc, are painful.

There are relatively few contraindications to performing ESIs. Absolute contraindications include bleeding diathesis and full anticoagulation because of the risk of epidural hematoma. Patients on anticoagulants must stop the medication and have their coagulation profile temporarily normalized before any minimally invasive procedure, if deemed medically appropriate to do so. Patients taking warfarin should hold this medication for 3 to 5 days and undergo laboratory analysis of their clotting factors immediately before the scheduled procedure [63]. If the risks associated with warfarin suspension are too great for precipitating a thromboembolic event, the patient can be covered by low dose heparin or a low molecular weight heparin while stopping the warfarin 5 to 7 days before the injection, restarting it 6 to 12 hours after the injection [63]. Nonsteroidal anti-inflammatory agents and aspirin do not need to be stopped before an injection [64]. However, the safety of ticlopidine (Ticlid™) and clopidogrel (Plavix™) has not been established and should be held 5 to 7 days and 10 to 14 days before an injection, respectively [63]. Other contraindications to ESIs include 1) local infection at injection site; 2) sepsis; 3) hypovolemia; 4) pregnancy; 5) uncontrolled diabetes; 6) uncontrolled glaucoma; and 7) high concentrations of local anesthetics in patients with multiple sclerosis [63].

Deposition of corticosteroid into the epidural space would not be appropriate in the setting of spinal infection, malignancy, or acute fracture. Chronic spinal fractures may not represent a contraindication to ESIs if the pain is likely discogenic in origin.

Currently, no data exist regarding predictive factors after ESIs for CLBP. The ideal patient for ESIs would have discogenic pain with provocative discography to demonstrate outer annular disruption causing the patients' usual symptoms, and internally sound, nonpainful adjacent discs serving as internal controls. A reasonable algorithmic approach to a patient presenting with CLBP most consistent with a discogenic etiology is to perform S1 TFESIs to empirically target the L4–5 and L5–S1 discs [61,65].

Evidence of efficacy

Systematic reviews

In 1994, a report was published by the Australian Working Party of the National Health and Medical Research Council summarizing recommendations for ESI in the management of LBP [62]. This summary statement referenced a body of evidence endorsing ILESIs and CESIs as viable treatment options for radicular pain. However, the report cited a minimal body of literature evaluating the use of ESIs for treatment of any form of nonradicular spinal pain [62]. A year later, Watts and Silagy published a meta-analysis of randomized trials demonstrating efficacy of blind CESIs and ILESIs for radicular, but not axial, LBP [66]. In 1999, Koes et al. performed a systematic review of randomized controlled trials (RCTs) of CESIs and ILESIs in patients with lumbar and/or sciatica [67]. The authors identified 15 RCTs, of which 50% found utility of these injections for lumbar and sciatic pain. However, the review found no clear indication that these injections might be effective for CLBP without radicular pain [67]. The most heavily weighted methodological study criteria identified by Koes et al. were large study groups, description of intervention, use of relevant outcome measures, and blinded outcome assessments. However, the investigators did not place a value on the techniques used by each study. Consequently, the technical flaws in each study—including lack of fluoroscopic guidance and contrast confirmation of accurate needle placement—were not properly analyzed. Others have also noted that these studies failed to adequately assess the technical shortcomings of non–target specific injections to treat inadequately diagnosed lumbar pain [68,69]. In a more recent review, DePalma et al. [70] assessed the efficacy and safety of TFESIs and selective nerve root blocks treating specifically lumbar radiculopathy.

Randomized controlled trials

Caudal epidural steroid injections

Six prospective RCTs have been published evaluating the efficacy of CESIs [71–76], only three of which evaluated lumbar pain [71–73]. Critical features of each study

that must be assessed are 1) route of injection (fluoroscopic control); 2) number of injections; 3) clinical presentation (LBP vs. radicular pain); 4) diagnostic evaluation (provocative discography); 5) length of follow-up; and 6) outcome measures.

Breivik et al. [71] in a prospective, double-blinded, crossover RCT assessed improvement in CLBP and sciatic pain in 35 patients treated with up to three blind CESIs of either bupivicaine and methylprednisolone or bupivicaine and normal saline. The study followed a parallel cohort design, allowing patients not benefiting from their randomized treatment to then undergo treatment in the reciprocal study arm. Initially, 56% of patients receiving methylprednisolone experienced significant relief compared with only 26% treated with bupivicaine/saline. In the crossover, 14% of the methylprednisolone group obtained relief from subsequent bupivicaine/saline injections, whereas 73% of the bupivicaine/saline group reported satisfactory relief after the methylprednisolone injection. Fifty percent of the methylprednisolone group and 20% of the bupivicaine group returned to work at a range of 3 to 17 months after treatment. Up to three injections were performed in each arm. Thirty-two patients had undergone radiculography demonstrating disc prolapse, arachnoiditis, or inconclusive findings. However, the CESIs were performed without fluoroscopic guidance, and no further diagnostic testing had been performed.

In a subsequent study, Yates [72] randomly assigned 20 consecutive LBP patients to CESIs with 1) saline; 2) lidocaine; 3) saline and triamcinolone; or 4) lidocaine and triamcinolone. Each patient was assessed at 30 minutes and again 1 week after each injection. Outcome measures included improvement in straight leg raising (SLR) and lumbar range of motion. Improvements were reported in both outcomes, with greater improvements noted after the injection of triamcinolone. Patients reporting greater than 50% improvement demonstrated significant improvement in lumbar range of motion and SLR. Yet, no specific diagnostic criteria were used in selecting patients for the trial, the follow-up interval was short, and few injections were completed.

In 1987, Mathews et al. [73] randomized 57 patients suffering from CLBP and sciatica to CESI (n=23) or local infiltration of lidocaine over the sacral hiatus (n=34). Three injections were completed reducing painful symptoms in 67% of CESI patients and 56% of control patients 1 month after the intervention; this difference was statistically significance at 3 months. Improvement remained greater in the CESI group through the 1-year follow-up, but the most profound difference was observed at 3 months. However, 16 CESI and 23 control patients required additional treatment. The diagnostic evaluation in that study was limited to blood work and lumbar plain films, the details of which were not reported.

The remaining three RCTs of CESIs [74–76] enrolled patients solely complaining of unilateral radicular pain and did not report on changes in axial symptoms. The investigations that assessed axial LBP demonstrated short-term efficacy of CESIs in treating lumbar pain with long-term benefits waning over time. However, these injections were not target specific, diluted the corticosteroid with large volumes of injectate, and were performed without fluoroscopic guidance. Furthermore, precision diagnostic evaluations were not used to confirm the presence of discogenic lumbar pain in the study subjects Table 1.

Only one study has prospectively evaluated the efficacy of CESIs in patients diagnosed with discogenic LBP by provocative discography [77]. Greater than 50% reduction in pain was achieved at 6 months after completing one to three CESIs in 60% and 64% of discogram negative and positive patients, respectively. Although each patient had undergone negative diagnostic facet joint and SIJ blocks with local comparative anesthetic, the investigators did not assess for concordantly painful outer annular disruption. A small number of patients comprised the discogram positive group. Unfortunately, neither the positive discogram levels nor the immediate post injection improvement in LBP were reported. The results of this study, despite using discography, do not confirm that CESIs are effective for discogenic lumbar pain.

Interlaminar epidural steroid injections

Ten controlled studies have been performed evaluating the efficacy of ILESIs [78–87]. Three studies [86–88] have investigated these interventions for axial lumbar pain, and seven evaluated ILESIs for radicular pain [78–84].

In a prospective, double-blinded RCT, Serrao et al. [86] studied the therapeutic effects of single injections of 80 mg methylprednisolone epidurally compared with 2 mg of intrathecal midazolam in 28 patients with CLBP. No statistically significant difference in pain or analgesic use was observed between the two groups at 2 months. The authors did not report details of their diagnostic evaluation of these patients, the segmental level at which each injection was performed, and fluoroscopic guidance was not used.

Years previously, Helliwel et al. [87] studied 39 patients with LBP and radicular leg pain in a single-blinded investigation. Twenty subjects underwent a single extradural injection of 80 mg methylprednisolone in 10 ml normal saline. These patients reported statistically significant reduction in pain levels at 1 and 3 months compared with 19 control patients who underwent an interspinous injection of 5 ml normal saline. However, the authors did not report at what level each injection was performed, and did not clarify if the pain scores were recorded primarily for LBP or radicular pain.

In an observational study, Buttermann [88] reported significant improvement in pain and function in 25% to 35% of CLBP (greater than 1 year) patients after performing one fluoroscopically guided ILESI or TFESI. Follow-up was carried out to 1 to 2 years. There was no indication regarding at which level each injection was performed. In addition to the absence of a control group, a high number of drop outs occurred as patients went on to other treatment

Table 1
Results of published investigations of lumbar ESIs in treating radiculopathy

Reference	Control group	Number of subjects	Number of injuries	Outcome tools	Relief at F/U compared with C	Results	Comments	Study quality
[71]	Bupiv/saline	35 (T=16, C=19)	1–3 CESI	Satisfactory pain relief; return to work	56%/26% 3–17 mo f/u	Positive	Crossover design with 14% compared with 73% of control improving after crossover	Good/Fair: No fluoroscopic guidance; No definitive diagnostics
[72]	Saline or lidocaine	20	1 CESI	Symptomatic improvement; SLR; lumbar ROM	Improvement with steroid 30 min and 1 wk	Positive	4 tx groups (saline, lidocaine, saline+steroid, lidocaine+steroid)	Fair: Only one injection offered; short follow-up interval; No fluoroscopic guidance; No definitive diagnostics
[73]	Local lidocaine	57 (T=23, C=34)	3 CESI	Pain level	67%/56% at 1–3 mo	Negative	16 of CESI and 23 controls required additional tx	Fair: Short follow-up interval; No fluoroscopic guidance; No definitive diagnostics
[86]	Intrathecal midazolam	28	1 TLESI	Pain level/ analgesic use	No difference at 2 mo	Negative	Prospective, double blind	Fair: short follow-up; only one injection performed; no fluoroscopic guidance
[87]	Interspinous saline	39 (T=20, C=19)	1 TLESI	Pain level	Statistically sign reduction over control at 1 and 3 mo	Positive	Single blind	Fair: One injection performed at undisclosed level; no fluoroscopic guidance; no definitive diagnostics
[94]	SP	160 (T=80, C=80)	1 TFESI	VAS, OLBDQ, NHP	Greater improvement at 3 and 6 mo in control group	Negative	Power analysis calculated; primary symptom radicular	Fair: One injection performed/patient; no definitive LBP diagnostics
[100]	Bupiv	86 (T=80, C=80)	1 TFESI	VAS, OLBDQ	No difference at 12 wk	Negative	HNP and foraminal stenosis–related radicular pain primary complaint	Fair: One injection performed/patient; no definitive LBP diagnostics; stenosis patients included

ESI=epidural steroid injection; Bupiv=Bupivicaine; C=control; T=treatment; TLESI=translaminar corticosteroid/anesthetic injection; TFESI=transforaminal epidural steroid injection; VAS=visual analogue scale; SLR=straight leg raising; Positive=significant improvement in symptoms because of treatment effect; Negative=no improvement because of treatment intervention; OLBDQ=Oswestry Low Back Disability Questionnaire; F/U=follow up; ROM=range of motion; HNP=herniated nucleus pulposis; NHP=Nottingham Health Profile; SP=saline placebo; 4tx=4 treatment groups.

Study quality: Good, Treatment and control injections prospectively randomized with one to three or four injections performed per patient. Patients blinded to injection contents. Control injections not truly placebo as anesthetic and saline have therapeutic effects; Fair, Randomized in prospective fashion without placebo injection. Control injection typically used therapeutically. Only one injection performed per patient; Poor, Interventions not randomized despite prospective data acquisition.

interventions including fusion surgery. Hence, the treatment effect may have been overestimated.

Results of these trials weakly clarify the efficacy of ILESIs for axial LBP, which may afford the patient only short-term improvements. However, ILESIs are not target specific, especially in the absence of fluoroscopy, and definitive diagnostic measures were not taken in these studies.

Transforaminal epidural steroid injections

TFESIs have been well studied in treating lumbar radicular pain [89–95], and one systematic review has been produced on this topic [70]. However, no well-designed study has evaluated the utility of lumbar TFESIs in treating axial LBP. Two studies [94,95] included assessment of LBP in addition to lower limb radicular pain.

Karppinen et al. [94] completed a double-blinded RCT of patients with lumbar radiculopathy because of a corroborative disc herniation who underwent a single TFESI at the indicated level. Although the study was designed to assess the efficacy of a TFESI for nerve root pain, the authors also evaluated lumbar pain. Each injection was performed under fluoroscopy with 2 to 3 ml of injectate at the level of clinical involvement. Only one injection was performed in each patient, with the treatment arm undergoing injection of 1 ml of 40 mg/ml methylprednisolone and 1 ml of 5 mg/ml of bupivicaine, and the control group underwent injection of 2 ml of isotonic saline. Eighty patients were enrolled into each group after a power analysis revealed a need for 68 patients in each study arm. No difference in immediate improvement in lumbar pain occurred between the groups. At 2 and 4 weeks, and 12 months follow-up, lumbar pain intensity was slightly less in the methylprednisolone group, but this did not reach statistical significance. At 3 and 6 months, statistically greater improvement in lumbar pain in fact occurred in the saline group.

Although the Karppinen et al.'s study used an appropriate number of subjects, the investigation did not ideally address the question of whether or not TFESIs are effective for discogenic LBP. Each patient's lumbar pain was presumably because of the disc herniation whose posterolateral annular fibers were reached by the injectate [35], affecting the treated nerve root. However, further diagnostic interventions such as provocative discography were not performed. The side of the annular disruption may not have corresponded to the side of symptom manifestation [95], and the axial pain symptoms may have actually represented proximal nerve root pain. Only one injection was completed in each patient, though more than one injection is frequently necessary to adequately treat radicular pain [89,96]. Similar evidence is lacking suggesting how many injections may be necessary to adequately treat discogenic lumbar pain. Epidural saline may have a greater therapeutic benefit [97–99] than placebo, thus underestimating a treatment effect in Karppinen et al.'s study. Long-term benefit may not have been achieved because of a subtherapeutic number of TFESIs performed in the treatment arm, lack of true placebo control (sham injection), and improperly targeting the correct level of axial pain generation.

Ng et al. [100] randomized 86 lumbar radicular pain patients in a double-blinded manner to either periradicular infiltration of 2 ml of 0.25% bupivicaine or 2 ml of bupivicaine and 40 mg of methylprednisolone. Inclusion criteria were patients with lower limb pain equal to—or greater than—LBP, and MRI evidence of a corroborative disc herniation or foraminal stenosis. Each patient underwent only one injection. Visual analog scale and Oswestry disability index were measured at weekly intervals up to 12 weeks, with a 100% follow-up rate. No difference was observed in outcomes at 12 weeks after one injection. It is difficult to derive conclusions from this study regarding the efficacy of one TFESI to treat axial LBP. Corroborative diagnostic evaluation such as discography was not performed. Patients with foraminal stenosis were included. These two factors may have diminished the likelihood of discogenic lumbar pain in a portion of enrolled patients. Patients requiring repeat injections were deemed treatment failures and removed from the study's follow-up. Therefore, a subtherapeutic number of TFESIs may have been undertaken.

Harms

Side effects associated with ESIs have been well studied and tend to be minor and transient [101–103]. They include 1) increased injection site pain (17.1%); 2) increased radicular pain (0.6%–8.8%); 3) light-headedness (6.5%); 4) increased spine pain (2.4%–5.1%); 5) nausea (3.7%); 6) nonpositional headache (1.4%–3.1%); 7) vomiting (0.5%); 8) facial flushing (1.2%); 9) vasovagal reaction (0.3%); 10) increased blood sugar (0.3%); and 11) intraoperative hypertension (0.3%) [101,103,104]. The overall incidence of minor, self-limited side effects associated with ESIs ranges from 5.5% [102] to 9.6% [104] with TFESIs to 15.6% with CESIs.

Potential side effects and complications may arise as a consequence of needle placement, the type of medications injected, and the use of X-ray guidance, the last of which is not a concern during the performance of blind ILESIs or CESIs. Reports on large series of lumbosacral ESIs reveal them to be relatively safe when performed correctly by well-trained physicians [89,101,102]. Catastrophic complications with ESIs are rare.

Any minimally invasive, percutaneous procedure involving a needle carries the risk of infection, but large case series have not reported such complications with ESIs [89,101,102]. Spinal injections carry the additional risk of inadvertent dural puncture, neural trauma, vascular injury, or central nervous system injury. Dural puncture occurs in 5% of ILESIs, 0% to 0.6% of CESIs [62,103], and 0% to 0.1% of TFESIs [101,102]. Puncture of the dural lining may result in a post-dural puncture headache related to the leakage of cerebrospinal fluid, though the complaint

typically self-limiting. Established measures for more persistent or severe headache include bed rest, increased fluid intake, and an autologous epidural blood patch. If recognized early, dural puncture is not a large concern when performing ESIs. However, injection of corticosteroid and anesthetic into the subarachnoid space can cause spinal anesthesia or arachnoiditis.

Intravascular uptake is possible after ESIs but can be eliminated with the proper use of contrast-enhanced fluoroscopic control. Intravascular injection has been demonstrated to occur in 6.4% to 10.9% of CESIs [32,36,105], 1.9% of ILESIs, and 10.8% to 11.2% of TFESIs [36,37] with a higher rate occurring at the S1 level [37]. A positive blood aspirate during the TFESIs is 97.9% specific but only 44.7% sensitive for predicting intravascular injection [37]. Intravascular injection of steroid and anesthetic can result in spinal cord injury [106] believed to occur because of injection into the artery of Adamkiewicz. The precise mechanism of injury is not completely understood but may involve arteriole vasospasm or embolization of corticosteroid particulate–induced ischemic injury. Therefore, fluoroscopic control using contrast confirmation of needle placement is mandatory to ensure safe and effective needle placement as evidenced by safe performance of large numbers of TFESIs [101–103].

Predictors of negative outcome after ESIs have been studied for ILESIs [107,108] when treating lumbar radicular pain. In an assessment of 209 patients, increased risk of treatment failure at 2 weeks after one to three injections was associated in univariate analyses with the following variables: 1) lower levels of education, 2) smoking, 3) unemployment, 4) constant pain, 5) chronic pain, 6) psychological disturbances, and 7) nonradicular diagnoses. Using logistic regression analysis, only prolonged duration of pain, nonradicular diagnosis, unemployment, and smoking were independently associated with a failed treatment outcome [107]. However, just 6% of the subject cohort presented with primarily axial, nonradicular pain. In a study of 249 LBP patients, Jamison et al. [108] excluded patients with psychiatric disorders and, using a multiple regression analysis, found that the following factors were associated with a poor outcome at 2 weeks after one ILESI: 1) increased number of previous treatments for pain, 2) more medication taken, 3) pain not increased by activities, and 4) pain increased by coughing. Whereas at 1 year after injection, pain not interfering with activities, unemployment because of pain, normal SLR before treatment, and pain not decreased by medication predicted no benefit after one ILESI. However, just 53% of treated patients were followed for 1 year and Jamison et al. injected 120 mg methylprednisolone whereas Hopewood et al. injected 50 mg of triamcinolone into the epidural space. Derby et al. also evaluated the prognostic capability of TFESIs [109]. However, these patients were treated for radicular pain rather than for axial lumbar pain, and the response to TFESIs was examined as a predictor of surgical outcome [109].

Summary

CLBP has recently become better understood, allowing an accurate diagnosis in most of the cases. The judicious use of fluoroscopically guided, contrast-enhanced, controlled diagnostic spinal procedures provides better direction for the use of target-specific therapeutic interventions such as ESIs. The specific identification of a particular lumbosacral structure responsible for a patient's symptomatology aids subsequent efforts to both treat injury of this structure and help prevent symptom exacerbation. The culmination of these findings is the premise that to best treat the different etiologies of CLBP, strategies specific to the implicated structure must be pursued. For example, painful lumbar z-joints would best be treated with therapeutic intra-articular injections or ablation of the joint's nerve supply. Injection of corticosteroid into the epidural space would not appropriately address the source of the symptoms. Injury of an anterior column component such as the intervertebral disc would suggest that instillation of a therapeutic agent into the anterior epidural space would maximize therapeutic benefit if such benefit is feasible. The most direct means by which to achieve anterior epidural spread is via a transforaminal approach. Hence, TFESIs are most appropriate in targeting discogenic pain after confirmation that the source of CLBP is an intervertebral disc.

No well-designed studies have been constructed to thoroughly assess the efficacy of TFESIs in treating discogenic CLBP. Consequently, definitive statements regarding their use for CLBP have been precluded. The evidence that is available suggests that non–target specific ESIs are effective for short-term improvement in nonspecific CLBP. Such injections are safe when performed by well-trained physicians and may reduce a patient's disability sufficiently to avoid more aggressive diagnostic and therapeutic options. Therefore, ESIs are a reasonable treatment option of CLBP unresponsive to physical therapy, anti-inflammatory medications, and a tincture of time. TFESIs are probably the best approach to instill corticosteroid into the anterior epidural space to treat painful lumbosacral intervertebral discs. Yet, this premise is founded on the conviction that inflammation plays a causal role in the production of pain emanating from a lumbar intervertebral disc.

One to three CESIs appear to be effective in reducing nonspecific CLBP in the short term. More definitive statements regarding efficacy of CESIs for discogenic CLBP and the duration of benefit cannot be made as such data has not been generated. A single ILESI may provide short-term relief from nonspecific CLBP; however, long-term improvement in nonspecific CLBP with ILESIs has not been founded. Transforaminal LESIs do not appear to be effective in reducing nonspecific LBP after performing just one injection in the absence of definitive diagnostic evaluation establishing discogenic LBP. However, conclusive statements regarding the appropriate role of CESIs,

ILESIs, and TFESIs cannot be made until better research protocols are developed.

A definitive study protocol aimed at assessing the utility of LESIs for axial LBP has not been engineered. Nonetheless, such a protocol must use target-specific injections to adequately reach the diagnostically proven intervertebral disc(s) responsible for clinical symptoms. Patients would be enrolled with CLBP recalcitrant to physical therapy, nonsteroidal anti-inflammatory medications, and adjunct analgesics. Plain film radiography and MRI must reveal intact osseous alignment with minimal listhesis, and demonstrate degenerative intervertebral disc changes. Subsequent provocative discography and post-discography CT must reveal corroborative outer annular disruption producing concordant lumbar pain, and a negative internal control. Instillation of corticosteroids should be performed via TFESIs targeting the affected disc(s). Performing one to three injections would be reasonable before deeming the treatment a failure. Timing of the injections may have a bearing on successful outcome and should be independently evaluated. Outcome measures should include measurement of pain, disability, analgesic intake, return to previous level of function or work, and avoidance of more aggressive treatment options such as surgery. Only a stringent protocol controlling for concurrent structural abnormalities (spondylolisthesis) while assuring proper identification of the discogenic source of pain will allow proper and accurate evaluation of the efficacy of ESIs in treating axial lumbar pain. Publishing whether or not patients experienced immediate improvement might help confirm if the ESIs adequately reached the putatively painful disc.

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