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Not All Conditions Respond Equally to Spine Injections: A Review of the Outcome Literature for Common Spine Pathologies

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Abstract A variety of spinal pathologies can result in symptoms including low back and radicular pain. These different diagnostic etiologies have different natural histories and may have varying responses to treatment. Unfortunately, this is not often accounted for in the literature, and the outcomes from treatment of these various diseases are lumped together based on their symptomology. This is an inappropriate way to examine the literature given the different pathologies. This article will therefore offer a narrative review of the outcomes of injection therapy for common disease processes including zygapophyseal (facet) joint pain, sacroiliac joint pain, discogenic pain, disk herniation with radicular pain, and spinal stenosis.

Keywords Epidural · Spine · Injections · Facet · Stenosis · Disk herniation · Radiculopathy · Low back pain

Introduction

Spinal pain is one of the most common reasons for physician's office visits. There are many causes of spinal pain. Most often, the etiology is benign with the physician left to determine the "source of the pain" rather than treating a systematic disease. It is believed that low back pain (LBP) in particular occurring as a result of disk degeneration starts at the intervertebral disk (IVD), with changes in spine forces that lead to Zygapophyseal (Z)-joint degeneration [1]. Each spinal segment is composed with the combination of an IVD anteriorly and the paired Z-joints posteriorly, creating the "three joint complex" of the Kirkardly-Willis Cascade described in 1983 [2]. The disk and the two Z-joints progress through stages of dysfunction, micro and macro-instability, and finally stabilization with each one affecting the whole "complex." Joint degeneration is thus a multifactorial process that is tied to degeneration of the IVDs.

Nachemson stated in 1990 that the cause of LBP is unknown in the majority of patients [3]. Eleven years after, Deyo and Weinstein stated that 85 % of patients with LBP cannot be given a precise pathoanatomical diagnosis [4]. This number was based on a consensus statement from the late 1970's, and fortunately the ability to provide a more clear diagnosis has improved with modern imaging techniques such as MRI and the use of fluoroscopically guided diagnostic injections. With these technologies, specific spinal structures can be targeted with anesthetic injections and then assessed as the source of pain. In order to consider a structure as a cause of spinal pain [5], the structure should be

(a) innervated with nociceptive fibers
(b) able to produce pain clinically seen and able to induce pain in normal volunteers
(c) susceptible to disease or injury known to cause pain
(d) able to have the pain eradicated by a targeted diagnostic injection to identify the structure as a cause of pain.

The purpose of this article was to assess how the different common potential pain generators respond to their respective interventional spine injection. For axial pain, the

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pathologies include Z-joint pain, sacroiliac joint pain, and lumbar discogenic pain syndrome. For referred leg pain, these etiologies include lumbar disk herniation with radiculopathy and lumbar spinal stenosis (LSS).

Zygapophysial Joint (Z-Joint) Pain

Although it is accepted that pain can originate from pathology of the Z-joint [6–8], how such pathology is diagnosed and treated controversial. Many publications discuss a myriad of physical exam findings, which may correlate with Z-joint pain, among the lumbar flexion [9], extension [9–12] lateral rotation [11], sitting [13], pain relief in supine position [9], paravertebral tenderness [10, 11, 14], and worsening of pain with valsalva maneuvers [9, 12]. Interestingly some of the same maneuvers and specifically flexion and valsalva haven been also ascribed to discogenic pain. Pain is usually axial but can be referred widely in a sclerotomal pattern which can often be confused with discogenic pain, radicular pain, or even sacroiliac-mediated joint pain. In the end, no historical finding, physical exam maneuver, or imaging study can definitively diagnose Z-joint pain [15]. For example, has been found that the extension-rotation test (i.e., Kemp test), which is widely used in clinical practice, has a 100 % sensitivity, but only 12 % specificity for the diagnosis of Z-joint pain using a double block paradigm [15].

Currently, it has been accepted that the diagnosis of Z-joint pain is thus most accurately demonstrated via applied diagnostic-specific spinal injections targeting either the joint or the nerves that innervates it (the medial branches of the dorsal ramus). The Z-joint IA block anesthetizes the Z-joint itself, whereas the MBB anesthetizes the nerve supply of the Z-joints. Dreyer et al. argued that by first testing patients with a "double block" technique, he could improve the outcome of those found eligible for the therapeutic injection procedures [16]. Based on controlled diagnostic blocks of Z-joints, in accordance with the criteria established by the International Association for the Study of Pain (IASP), Z-joints have been implicated as responsible for spinal pain in 15–45 % of patients with LBP [17]. These numbers are obtained from studies that rely mostly on interventional means to diagnose Z-joint pain as the standard.

Unfortunately, the literature is limited that supports the efficacious use of intra-articular (IA) Lumbar Z-joint injections. In uncontrolled studies, the long-term relief of back pain after IA steroid injections ranges between 18 and 63 % [18, 19]. In the controlled studies in the literature, results are even more mixed. Whereas Lilius et al. [20]. reported no differences in outcome between the placebo and steroid groups, Carette et al. [21]. showed a significant improvement after 6 months in the steroid group. In the other hand, Lakemier did a randomized, double-blind, controlled trial which revealed relief of Z-joint pain, and functional improvement can be achieved by medial branch neurotomy and IA Z-joint steroid injections. However, no significant differences were noted between the two procedures. In that study, they included. Only patients with Z-joint pain involving the L3/L4–L5/S1 segments who had significant pain relief after a single IA diagnostic injection with local anesthetic. Therefore, this study demonstrated that patients with Z-joint pain as confirmed by a single IA anesthetic injection can be treated with IA steroid injections or medial branch neurotomy with appropriate pain relief and functional improvement over a period of at least 6 months, with no differences between treatments [22].

Collectively, this literature has lead to reviews not recommending IA therapeutic injections as the literature supporting their efficacy is "weak," and the procedures were "not recommended at all" [23]. Therefore the main reason for these procedures continued use is the rationale to treat inflammation due to osteoarthritis that is suspected within the degenerated Z-joint. In other peripheral joints, there is substantial evidence that IA joint injections lead to improvement in function along pain relief [24, 25].

The literature on IA steroid injections stands in contrast to the evidence for radiofrequency neurotomy of the medial branches, which has a robust body of literature showing efficacy. Dreyfuss et al. [26] did an observational study on lumbar radiofrequency denervation medial branches innervating the Z-joints that consisted of 15 patients. After a rigorous evaluation, 41 subjects underwent diagnostic lumbar MBB with 2 % lidocaine. 22 of the 41 patients reported at least 80 % improvement in their index pain. Then they underwent a second comparative block using 0.5 % bupivacaine. 15 out of 22 had a positive response of at least 80 % pain reduction, hence having a diagnosis of Z-joint-mediated pain. Those 15 patients underwent a lumbar medial branch neurotomy. In terms of pain relief, 13 out of 15 patients (87 %) had 60 % pain reduction at 12 months. 9 out of 15 patients (60 %) had at least 90 % pain reduction at 12 months.

Another observational study was published by Gofeld [27] which was a prospective 10-year study. Patients were monitored at 1.5, 6, 12, and 24 months following the lumbar medial branch neurotomy. 174 patients completed the study. The results showed that 119 of the 174 patients reported good to excellent pain relief are 6 months after the medial branch neurotomy. 25.9 % of patients were classified as having excellent relief, with more than 80 % pain reduction. 42.5 % of patients had good pain relief with over 50 % pain reduction. 31.6 % of patients did not have significant pain reduction after 6 months following the procedure; therefore, the effect was less than 6 months.

Of the 174 patients, the median pain relief was 9 months. However, when only the 119 positive responders, who had pain relief over 6 months, the median pain relief was 12 months with 99 of them able to decrease the use of analgesics. Others have repeated these results in both the cervical and lumbar spine in larger numbers of patients [28•, 29•].

In summary, the outcomes for IA steroid injections while trending toward efficacy are not definite. This is in contrast to medial branch neurotomy which has been repeatedly shown to be very effective for Z-joint-mediated pain when patients are appropriately selected. The outcomes are more favorable when strict criteria of having the procedure if the diagnostic injections provide them over 80 % pain reduction and good understanding of the anatomy and correct needle placement are observed. More studies are needed to confirm these results.

Sacroiliac Joint (SIJ)-Mediated Pain

SIJ-mediated pain has been found to occur in 16–30 % of patients with LBP [30]. Presently, there is no specific history or physical examination findings that will prove the diagnosis of SIJ pain [31–33]. Slipman found that 44 % of SIJ patients had a traumatic event, 21 % had a cumulative injury, and 35 % had a spontaneous onset of SIJ pain [33].

Slipman [34] also found that the most common referral area is the buttock, which accounted for 94 % of the patient population. However, the pain commonly referred with 72 % having lower lumbar pain, 25 % reporting associated lower extremity pain most commonly in the posterior or lateral thigh, and 14 % having groin pain. Fortin et al. [35]. previously described pain referral zones resulting from provocative IA injections, with the common area of resultant pain being located over the posterior superior iliac spine (PSIS), which extends 10 cm caudally and 3 cm laterally.

The diffuseness of the SIJ pain referral zones may arise for several reasons: (1) the joint's innervation is highly variable and complex; (2) pain may be referred in a sclerotomal fashion; (3) adjacent structures may be affected by intrinsic joint pathology and become active nociceptors; and (4) pain referral patterns may be dependent on the distinct locations of injury in the sacroiliac joint [34].

It is also accepted that physical examination is somewhat limited in the ability to confirm SJI pain. Slipman [36] and Dreyfuss [32] found that neither the history nor positive SIJ provocation tests in isolation or in combination confirm a diagnosis of SIJ-mediated pain. Findings obtained during clinical evaluation allow progression through a diagnostic algorithm that culminates with a fluoroscopically guided SIJ injection. It is therefore accepted that a fluoroscopically guided diagnostic IA SIJ administration of local anesthetic represents the current standard test to confirm the diagnosis of SIJ-mediated pain [30–32, 37].

Given the challenges that arise in the diagnosis of SIJ pain, assessing the literature is difficult. Most studies did not screen appropriately and merely injected people with suspected SIJ pain. In fact, a definitive study on SIJ pain is still lacking. However, some literature does exist to help shed light on the topic. A retrospective study from Slipman [38] assessed the improvement of IA SIJ injection with corticosteroids and physical therapy to treat patients who had a prior IA diagnostic SIJ injection with at least 80 % pain relief. Patients' symptom duration ranged from a minimum of 1.5 months to a maximum of 84 months (average 20.6 months). Those patients underwent an average of 2.1 injections. At the mean follow-up (94.4 weeks), pain scores in a Visual Analog scale (VAS) were reduced by 43 %. The limitation of this study was the retrospective approach and lack of a control group. Liliang et al. [39] studied 39 patients using IA corticosteroids who had symptoms of SIJ-mediated pain. Those patients already were diagnosed by a dual injection paradigm. They had at least 75 % pain reduction for 1–8 h on both blocks. 26 patients (66.7 %) who underwent a corticosteroid injection experienced more than 50 % pain reduction for more than 6 weeks. The overall mean duration of pain reduction was 36.8 ± 9.9 weeks (range 12–60 weeks). The remaining 13 patients (33.3 %) who had a short term response to the corticosteroid injection, the mean duration of pain reduction was 4.4 ± 1.8 weeks (range 1–6 weeks). Collectively, these studies tend to show an effect of these interventions but definitely highlight the need for more research in this area.

Lumbar Discogenic Pain

The primary indication for ESI is radicular pain. Despite scant literature evidence for its use in axial back pain, many practitioners will still employ ESI for presumed discogenic pain [40]. Discogenic LBP accounts for approximately 39 % of the cases [41]. The most intuitive way will be via transforaminal route as the corticosteroid is been deposited in the anterior epidural space at the disk–nerve interface.

Manchikanti et al. [42] conducted a prospective randomized control trial. A caudal approach was utilized in their study, and patients were diagnosed with discogenic back pain with a provocative lumbar discography. Sixty percent of the patients who had a negative discogram and 64 % of patients with a positive discogram achieved more than 50 % pain reduction between 1 and 3 caudal injections. However, it was not mentioned in the study if the

patient had immediate post-injection improvement in their pain score. Also having a negative discogram and achieving a positive response does not classify the patient has having a truly discogenic pain. Therefore, this study cannot quantify if caudal ESI is effective for lumbar discogenic pain.

Buttermann [43] investigated in a prospective randomized control trial if ILESI are effective in lumbar degenerative disk disease (DDD). ILESI were performed in 93 patients with lumbar DDD along with inflammatory endplates changes versus 139 patients without endplate changes. Discography was carried out in 78 patients with inflammatory changes and 93 without inflammatory changes who were already considered surgical candidates for fusion. Buttermann pointed out that ESIs were effective in improving function and pain at short term. It was also found that patients with inflammatory endplate changes had greater improvement with the ODI and pain diagrams scores in the first 6 months following the procedure as compared to the patient without inflammatory endplate changes. At the 2-year mark approximately, one-third of the patients had no additional treatments. However, there was a drop out of 60 % of patients, and nearly one-third of the patients without inflammatory changes underwent a fusion surgery.

Lee and colleagues [44] compared bilateral TFESIs versus ILESI in 93 patients with herniated disk and 99 patients with spinal stenosis with only axial back pain. Patients underwent a single injection. Both approaches yielded significant pain relief between 2 weeks and 4 months in both group of patients. Patients with spinal stenosis had a significant reduction in the Roland 5-point pain score and obtained a better numerical rating scale with a TFESI versus the ILESI. Patients with herniated disks did not show any significant difference between the interlaminar versus a transforaminal approach.

In summary, although this is the most prevalent spinal condition in young patients, the evidence in terms of outcomes for lumbar discogenic pain is still unclear, and more studies should be considered.

Disk Herniation with Radiculopathy

Patients suffering from acute LBP with or without radicular symptoms often resolve their symptoms without any particular treatment. Approximately, 60–70 % of patients recover in 6 weeks, while 90 % of patients may achieve recovery in 12 weeks [45]. The use of ESI has a role if the acute or subacute radicular pain is severe and not responsive to medications or if the symptoms persist after a trial of conservative management.

Multiple studies have repeatedly shown that lumbar TFESI are effective in the treatment of radicular pain due to a HNP [46••]. This is highlighted by a five-arm placebo-controlled RCT, comparing intramuscular steroid, intramuscular saline, transforaminal steroid, transforaminal saline, and transforaminal lidocaine [47]. While only having 150 subjects, this study was powered to show statistically and clinically meaningful differences in those treated with transforaminal steroid. Additional analysis showed that duration had no effect on treatment outcomes, but exceedingly large disk herniations may respond less well [48]. Other studies including one by Vad have also found TFESIs to be superior to paraspinal trigger point injections with saline for radicular symptoms from HNP [49]. The primary strengths of this study include the length of follow-up (1.4 years) and the control intervention (a trigger point injection without any therapeutic epidural effect). The main flaw of this study was that the study was not blinded. Nevertheless, it was found that patients with radicular symptoms from HNP benefit from TFESI over placebo for both short- and long-term pain reduction and disability.

Other studies have also evaluated if these injections can prevent a more invasive spinal surgery. Riew et al. [50] evaluated at this issue by randomizing patients considered surgical candidates to receive either bupivacaine alone or bupivacaine combined with corticosteroid. All subjects had radicular pain secondary to HNP or either central or neuroforaminal stenosis. Initially, a significantly higher rate of surgery was found in the bupivacaine alone group compared to the bupivacaine plus steroid group. In a 5-year follow-up study, Riew demonstrated that most subjects who avoided surgery with the initial intervention did not progress to surgery [50]. This study suggests that TFESI can help patients to avoid surgery in many instances in patients with HNP who present with radicular pain.

In summary, lumbar HNP with radiculopathy has a favorable outcome due to the natural course of the disease. In patients with persistent pain, the literature demonstrates that many can respond significantly well with use of epidural injections. More specifically, better responses are being shown with the use of TFESI due to the ventral placement of the medication as compared to the ILESI and caudal ESI.

Lumbar Spinal Stenosis

Patients with LSS often present with either radicular pain or with symptoms of neurogenic claudication (i.e., pain with walking and standing that relieves with forward flexion of the spine and/or sitting). These symptoms can cause significant disability. Usual initial treatment consists of medical and rehabilitative management including a trial of medications and physical therapy. Failure of this leads to consideration of ESI treatments. On those who fail, a

surgical decompression is the other alternative. Outcome studies have looked into the outcomes of both surgical and non-surgical options. Interestingly, there is no study that correlates the non-surgical management with radiographic severity, although one study [51] showed that patients with scoliosis tended to have poorer outcomes with ESI.

In the Maine Lumbar Spine Study, patients presenting with LSS reported better outcomes with surgery than with conservative management at 1 and 4 years [52, 53]. However, surgical outcomes declined to some degree over time, and outcomes of patients who had conservative treatments improved somewhat with time. Also, surgery may be contraindicated in some patients suffering from LSS due to significant medical comorbidities. Therefore, conservative management remains a needed and viable alternative for those who cannot or do not want to undergo surgical management.

Delport et al. [54] evaluated LSS patient using either TFESI or caudal ESIs under fluoroscopic-guidance. ESIs provided approximately one-third of the patient population with more than 2 months of relief and more than one half with improvement in function. The surgical rate of was 20 %. The majority of patients were satisfied with ESIs as a form of treatment in assisting them through the more painful periods of their condition, although many required having another injection for periodic flare-ups over the 3-year span.

Weinstein et al. [55] conducted the surgical versus nonoperative treatment for LSS 4-year results of the Spine Patient Outcomes Research Trial (SPORT). It was concluded that patients with symptomatic LSS treated surgically compared to those treated conservatively maintain statistically significant improvement in pain and function over 4 years.

Finally, Friedly et al. [56••] conducted a double-blind, multicenter randomized control trial in which 400 patients were evaluated with central LSS and moderate-to-severe leg pain and disability to receive ESI of corticosteroids 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. At 6 weeks, there were no significant between-group differences. It was concluded treatment of LSS, ESIs with corticosteroid plus lidocaine offered minimal or no short-term benefit as compared with an epidural administration of lidocaine alone. However, while representative of current treatment trends in the United States, this study had several flaws including significant heterogeneity of patients and treatments. For example multiple degrees (mild, moderate, severe) stenosis were included and patients received different medications via different routes. All of this significantly limit the ability to interpret this study. However, collectively, the literature on injections for spinal stenosis is less favorable than for that of disk herniations.

Conclusion

The quality and outcomes of the efficacy literature for interventional treatments for various spine pathologies vary widely. Multiple well-designed studies have shown a very favorable outcome with a lumbar TFESI for radicular pain due to a HNP and with radiofrequency neurotomy for Z-joint pain. Other conditions that are frequently injected including SIJ pain, spinal stenosis, and discogenic back pain suffer from a lack of quality research. Thus, we are left wondering if there might be a subgroup that benefits from these procedures. We eagerly await future studies with appropriate inclusion criteria, statistical design, and outcome measures to help practitioners answer these questions.

Compliance with Ethics Guidelines

Conflict of Interest Jose Mena is a consultant for iFuse. Andrew Sherman declares that he has no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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