

Randomized Trial

Concordant Provocation as a Prognostic Indicator During Interlaminar Lumbosacral Epidural Steroid Injections

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Background: Interlaminar epidural steroid injection is a well-established intervention for the treatment of radicular pain. Pain is commonly reported during the injection into the epidural space; this provocation is typically either concordant or discordant with the patient's baseline pain. It is not well known how this provocation pain relates to treatment outcomes.

Objective: To determine the relationship between concordant versus discordant provocation during interlaminar epidural steroid injection and its effects on pain reduction at follow-up.

Study Design: Secondary analysis of a single center, prospective randomized double-blind study.

Methods: Interlaminar epidural steroid injections under fluoroscopic guidance were performed on 48 patients with radicular lumbosacral pain. After injection with 80 mg methylprednisolone and 2 mL of normal saline at a single level, patients were asked to report if pain was provoked, and whether the pain was concordant or discordant with their baseline pain. The primary outcome measure was self-rated percentage of pain reduction from baseline at 2-week follow-up. Secondary outcomes included improvement in activity level and decreased analgesic consumption.

Results: Provocation was observed in 37 out of 48 patients (77%). This was further classified as concordant (22/37, 60%) or discordant (15/37, 40%) pain. The concordant group achieved a significant decrease in self-reported pain as compared to the discordant group at 2-week follow-up (61%, $t = 2.45$, $P < 0.01$). There were also significantly more patients in the concordant group who reported 75% pain reduction as compared to the discordant group ($X = 6.44$, $df(1)$, $P < 0.05$). There were no significant differences between concordant and discordant groups in regard to improvements in activity level ($X = 2.56$) and decreased analgesic use ($X = 3.28$).

Limitations: The secondary analysis did not examine long-term outcomes.

Conclusions: The concordant group demonstrated significantly higher pain reduction as compared to the discordant group. There were no significant differences between the 2 groups in terms of improved function or reduced analgesic requirements. Concordant provocation during interlaminar epidural injection may be a predictor of outcome.

Key words: Lumbar epidural steroid injection, steroids, interlaminar injection, lumbar, lumbosacral, provocation, pressure paresthesia, low back pain

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Epidural steroid injection is a well-established intervention for the treatment of discogenic and radicular spine pain. Interlaminar and transforaminal techniques are used in clinical practice worldwide by interventional physicians (1-4). There is no

consensus regarding whether these epidural injections provide long-term benefit (3,4-6). However, several studies have shown that both techniques provide short-term pain relief, reduce the need for hospitalization, decrease opioid analgesic requirements, and increase

positive perception of global function from weeks to months (7-9). Thus, epidural steroid injections have become part of a multimodal approach, along with analgesics and physical therapy, in the acute and chronic management of lumbar back pain and radiculopathy (1-2).

Mechanical causes of lumbar back pain such as disc herniation and annular tears initiate the release of inflammatory cytokines and other mediators that lead to nerve root irritation. This inflammatory cascade is a critical component of pain generation at the interface of the nerve root and intervertebral disc. Epidural steroid injections are often done to help reduce the pain caused by these events, and are often a combination injection of steroid, local anesthetic, and/or saline solution (1-4). The overall concentration of inflammatory mediators may be reduced by the irrigative/washing out effect of injected volume into the epidural space. The steroids in the injectate may help reduce this pain through multiple anti-inflammatory mechanisms: steroids inhibit aggregation of leukocytes, reduce edema and stabilize cell membranes, suppress immune responses, and reduce synthesis of prostaglandins (10,11). Furthermore, it may prevent the release of inflammatory mediators including phospholipase A₂, substance P, and TNF-alpha (12). Steroids also interact with norepinephrine and serotonin neurons in the dorsal horn to suppress physiologic response to noxious stimuli, which may have an additive effect to reduce pain (11-12).

Local anesthetics block the activity of voltage-gated sodium channels, thereby inhibiting nerve impulse conduction along axons and reducing acute nociception (13). Local anesthetics, usually used in combination with the steroid, as an injectate medium have also been shown to have an effect on reducing nerve excitement by inhibiting nerve impulse propagation and provide membrane stabilization when radiculopathy is present (14). Local anesthetics have also been hypothesized to induce plastic changes in sensory and dorsal horn neurons and interrupt sympathetic activation (14). The analgesic effects of local anesthetics have been found to be prolonged beyond their half-lives and thus may have inhibitory action on other molecules in the neurologic circuit such as sodium, potassium (15-16), and calcium channels (17); TRPV1 (18); and bradykinin receptors (19). Local anesthetics may also attenuate the chemotactic response of neutrophils, thus reducing inflammation (20).

Patients have reported painful paresthesias during

injection into the epidural space. This provoked pain has been described as being in the same distribution as the patient's baseline pain (concordant) or dissimilar in both quality and distribution (discordant). For decades, physicians have anecdotally believed that concordant pain reproduction during epidural injection may be a positive prognostic sign (21). Few previous studies have examined this observation in terms of treatment outcomes. A recent study, by Candido et al (22), showed concordant provocation during interlaminar injections was associated with better and longer pain relief at follow-up.

In this secondary analysis of a randomized, double-blind study, we will assess the role of provocation pain as a possible prognostic indicator for the efficacy of interlaminar epidural steroid injection in treating radicular pain and seek to validate the findings in the recent study by Candido et al (22). This secondary analysis will investigate the incidence of provocation during interlaminar injection and assess whether concordant versus discordant paresthesias correlate with self-reported outcomes of pain reduction, activity levels, and medication intake at follow-up. The current hypothesis is that an experience of concordant pain during injection leads to better outcomes at follow-up and we seek to confirm this with our data.

METHODS

Patients

This investigation is a secondary analysis of a prospective randomized double-blind study of the short-term benefit of interlaminar and transforaminal epidural steroid injections. It received approval from the Institutional Review Board. In the initial study, patients were randomized to receive either interlaminar or transforaminal steroid injections. This secondary analysis of our database includes 52 patients who received interlaminar lumbar epidural injections only.

Patients were initially referred to the outpatient pain clinic by a group of specialists including neurologists, neurosurgeons, orthopedic surgeons, and rheumatologists that were familiar with the selection criteria. All patients were 18 years or older with a chief complaint of low back pain radiating to one or both lower extremities to a level below the knee. These patients had all failed conservative therapy, including trials of pharmacologic analgesic agents, physical therapy, and elapsed time. No patient had undergone epidural steroid injections in the previous 6 months

or back surgery. Standard evaluation prior to epidural injection included clinical history, physical examination, and radiologic imaging that included an x-ray series (anterior-posterior, lateral, flexion, extension) of the lumbar spine and magnetic resonance imaging/computed tomography (MRI/CT) of the lumbosacral spine performed from the time of pain onset.

Inclusion criteria (Table 1) were ability to read and write in English, chief complaint of low back pain with radiation to one or both lower extremities to a level below the knee, failed medication and nonpharmacological trial of one month, duration of back pain greater than one month, and correlation of clinical symptoms and signs with radiologic imaging.

Exclusion criteria (Table 1) were patients with cauda equina syndrome; pregnancy; history of arachnoiditis; spondylolisthesis (> grade 1), spondylolysis, progressive neurologic deficit; active malignancy; history of substance abuse or current psychiatric comorbidity; central spinal stenosis; previous lumbar back surgery; epidural steroid injections in previous 6 months; medicolegal or workman's compensation proceedings; and contrast, steroid, or local anesthetic allergy.

Prior to the first epidural injection, the evaluating physician performed a baseline assessment that consisted of a visual analog scale with numerical rating scale superimposed; analgesic medication intake; pain pattern with radiation; straight leg raising exam; and a focused physical exam including motor, sensory, and reflexes. The findings of this pre-injection assessment were correlated with imaging studies.

Interlaminar Epidural Steroid Injection Technique

A single attending physician performed all epidural steroid injections. This eliminated any possible

inter-physician variability in technique and efficacy. The evaluating physician determined the level and side of the injection to best treat the radicular pain based on the patient's symptoms and radiologic presentation. The patient was positioned prone without sedation and the superior border of the inferior lamina was marked at the desired level. Overlying skin was infiltrated with 1% lidocaine and an 18 gauge Tuohy needle was guided until the needle was engaged in the supraspinous ligament or deeper. Loss-of-resistance was the primary sign of entry into the ipsilateral epidural space. When loss-of-resistance was obtained using air, lateral fluoroscopic images were obtained to ensure that the needle tip was positioned along the posterior border of the spinal canal. Epidural placement ipsilateral to the side of the chief complaint was confirmed by injecting iohexol contrast medium in one mL increments. The patient was notified they would be getting the therapeutic injectate, which consisted of 80 mg of methylprednisolone and 2 mL of normal saline. After the therapeutic injection, the patient was asked to report if they experienced pain during the injection and if the pain was similar or different to their baseline pain.

Outcome Measures

The primary outcome measure of this study was self-rated percentage of pain reduction from baseline. Secondary outcome measures included improvement in activity level and decreased daily analgesic intake. The evaluating physician reassessed each participant 10 – 16 days following the epidural injection with the "ESI Follow-up Evaluation Form." This form recorded pain reduction as a self-rated percentage, changes in functional activity, and daily analgesic consumption.

Table 1. *Inclusion and exclusion criteria.*

Inclusion Criteria	Exclusion Criteria
Chief complaint of low back pain radiating to one lower extremity	Previous lumbar spine surgeries or epidural steroid injections in the previous 6 months
Failed analgesic and nonpharmacologic therapy trial of at least one month	Multilevel degenerative spine disease, unstable spine, spondylolysis
Duration of current back and leg pain for greater than one month	Cauda equina syndrome, arachnoiditis, progressive neurologic defect
Symptoms due to acute, or subacute, disc disease	Spinal stenosis, vertebral compression fractures
Correlation between the clinically determined level (s) of radiculopathy and the findings on CT or MRI	Active cancer, history of substance abuse, current psychiatric comorbidity, pregnancy
Inability to tolerate physical therapy or no benefit from ongoing physical therapy	Myelographic contrast allergy, steroid allergy, local anesthetic allergy

Statistical Analysis

The sample size for this study was 52 patients. The self-rated percentage of pain reduction was used as the primary measure for efficacy of the epidural injection. This study also analyzed a 75% reduction in pain scores as a more robust measure of clinically significant improvement. A one-tailed independent student's T-test was used to compare the continuous variable of pain reduction in both concordant and discordant groups. Results were considered statistically significant if the P level was less than 0.05. Chi square analysis was used to test the relationship of the secondary outcome measures of improvement in functional activity and baseline daily analgesic consumptions.

RESULTS

A total of 52 patients with low back and radicular pain were enrolled in this study. Of these, 4 patients were excluded due to history of central spinal stenosis or previous back surgery. The most common diagnosis of patients that met inclusion criteria was intervertebral disc herniation. Forty-eight participants with a mean age of 48.3 years +/- 12.6 years were administered interlaminar epidural steroid injections and were included in the final analysis. Most injections were performed at L4-L5 (48%) or L5-S1 (48%), the rest were at L3-L4 (4%).

All patients were asked during the injection whether pain was provoked. The patients were then asked if the pain was in the same distribution as their baseline pain (concordant) or dissimilar in both quality and distribution (discordant). Provocation paresthesias were observed in 37 out of 48 patients (77%), while the remaining 11 reported no provocation during injection. Of these, 22 patients reported concordant pain (60%) and 15 reported discordant pain (40%).

At 2-week follow-up, the concordant group achieved a significant decrease in self-reported pain as compared to the discordant group ($t = 2.45$, $P < 0.01$). There were also significantly more patients in the concordant group who reported 75% or greater pain

reduction as compared to the discordant group ($X = 6.44$, $df(1)$, $P < 0.05$). The concordant group showed a significant decrease in self-reported pain ($t = 1.71$, $P < 0.05$) when compared to the non-provocation group, with significantly more also reporting 75% or greater pain reduction ($X = 3.95$, $P < 0.05$).

In terms of secondary outcomes, 22 patients with provoked pain reported improved activity (61%) and 19 patients reported decreased daily medication intake (51%). There were no significant differences between patients with concordant and discordant paresthesias in regard to improvements in activity level ($X = 2.56$) and decreased analgesic use ($X = 3.28$) at the 2-week follow-up mark (Table 2). Additionally, there were no significant differences between the concordant and non-provocation groups for improvements in activity level ($X = 2.356$) and decreased analgesic use ($X = 0.989$).

In summary, patients who reported a concordant paresthesia during injection had a statistically significant decrease in self-rated pain compared to patients who reported either a discordant or no paresthesias. There were also significantly more patients in the concordant group that reported 75% or greater pain reduction. There were no significant differences between groups for improvement in activity level or decreased daily analgesic intake.

DISCUSSION

This secondary analysis of a randomized, double-blind study investigated provocation and patterns of concordance during interlaminar epidural steroids injections. It included participants with acute or sub-acute lumbar pathology with unilateral or bilateral radiculopathy. These patients were divided into concordant or discordant groups during follow-up based on their initial feedback during injection; both the physician and patient were blinded to the above measures. The average age was similar between patients reporting discordant versus concordant paresthesias during injection and there was no noted difference between

Table 2. Outcomes for the entire population and by group.

Type of Provocation	% Pain Reduction	Greater than 75% Pain Reduction	Improvement in Activity	Decrease in Medication Use
All patients N = 37	50%	14 (38%)	22(59%)	19 (51%)
Concordant N = 22	61%	12 (55%)	16 (73%)	14 (64%)
Discordant N = 15	34%	2 (13%)	6 (40%)	5 (33%)

genders. Provocation was observed in 37 out of 48 patients (77%). Of these, 22 patients reported concordant pain (60%) and 15 reported discordant pain (40%).

As previous literature has shown, epidural steroid injections have short-term pain benefits (1-4,23-25). We focused on the short-term outcome that included self-reported pain percentage reduction as our primary measure. At follow-up, those patients who reported concordant pain during injection achieved a significant decrease in self-reported pain as compared to those who had discordant or no paresthesias. This observation was particularly strong as it remained valid with an alpha level as low as 0.01. As a more robust measure of clinically significant improvement,

this study used a level of > 75% reduction in self-rated pain scores. We found that there were significantly more patients in the concordant group who met this criterion as compared to both the discordant and non-provocation groups.

This secondary analysis used improvements in activity level and decreased opioid analgesic intake as secondary outcomes. Most patients did report improvement in these secondary outcomes regardless of provocation. However, we found that there were no significant differences between patients who reported concordant, discordant, or no paresthesias in regard to improvements in activity level or decreased opioid analgesic use at follow-up (Figs. 1-2).

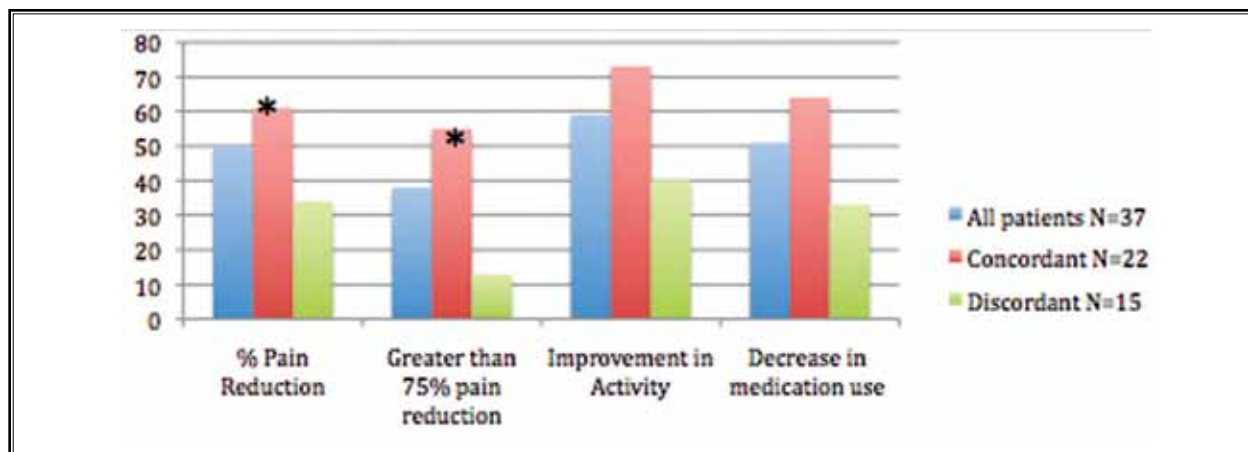


Fig.1. Outcome comparison for concordant versus discordant groups at follow-up (* = statistical significance).

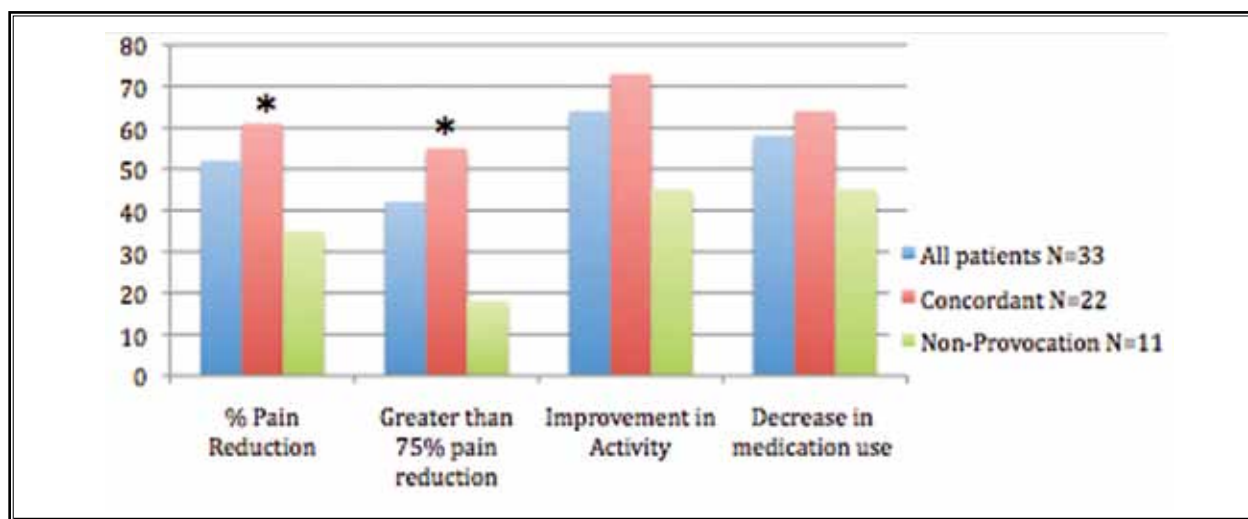


Fig.2. Outcome comparison for concordant versus non-provocation groups at follow-up (* = statistical significance).

There is limited literature on provocation during epidural steroid injections. It was first described by William Evans in 1930 that patients who experienced more radicular pain during epidural injection had favorable results (21). Schwartz et al (26) investigated the relationship between pain provocation and the analgesic response in 203 lumbar zygapophyseal joint blocks. The study found that reproduction of similar pain using liberal criteria of provocation correlated with improved pain relief after a single analgesic block (26). However, they found no significant association when more stringent criteria of provocation were adopted. Palastaras et al (27) found that reproduction of a patient's typical radicular pain during transforaminal lumbosacral epidural injection did not predict a significant decrease in pain scores—in fact, they found patients with concordant pain during injection had a trend towards worse pain relief at follow-up.

A recent study by Candido et al (22) showed that concordant provocation during interlaminar injections was associated with better and longer pain relief at follow-up. The findings of our current study would seem to confirm their results. The reproduction of usual, daily pain (concordance) during interlaminar epidural steroid injections may indicate proper delivery of medication to the target. Thus, concordant provocation may be a positive prognostic indicator of pain relief at follow-up following epidural steroid injection.

Limitations

The limitations of our analysis include sample size, a single interventionalist performing all injections, and a lack of long-term follow-up and end points. It is possible that a larger sample size could see differences for both the primary and secondary outcomes. Performance of all injections by a single interventionalist could have decreased outcome variability in the study. We also did not investigate common long-term outcome end points such as back surgery and economic factors. A follow-up

period of at least 6 months would have also allowed us to better assess the long-term effects of provocation during epidural injections on outcome. Previous studies on epidural injections using local anesthetic with or without steroids have demonstrated pain relief even up to 2 years of follow-up with epidural injections (5,28,29). It would be interesting in future studies to see if the occurrence of concordance during injection has any long-term benefits.

Another possible limitation was that our injectate did not contain local anesthetic, which is common practice, but rather only steroids and sodium chloride. Multiple studies have demonstrated only modest superiority of an injectate composed of steroids and local anesthetic during epidural injections when compared to local anesthetics alone in short-term follow-up (5,28,30). However, the main objective of our analysis was to determine if the type of mechanical provocation caused by epidural injection or non-provocation mattered in short-term outcomes and whether it has prognostic value. The action of local anesthetic added to the injectate could potentially diminish the sensation of provocation.

CONCLUSIONS

In summary, we investigated provocation during interlaminar epidural steroid injections for low back pain with radicular symptoms. We compared the differences in short-term clinical outcome for patients who reported feeling their usual, daily pain during injection to those who had atypical pain during injection. The results showed that patients who reported concordant pain achieved a significant decrease in self-reported pain as compared to those who had discordant paresthesia, which is consistent with the results of previous studies. We conclude that concordant provocation during interlaminar epidural steroid injections may be a positive prognostic factor for short-term pain relief.

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