Fluoroscopic lumbar interlaminar epidural injections in managing chronic lumbar axial or discogenic pain

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Abstract: Among the multiple causes of chronic low back pain, axial and discogenic pain are common. Various modalities of treatments are utilized in managing discogenic and axial low back pain including epidural injections. However, there is a paucity of evidence regarding the effectiveness, indications, and medical necessity of any treatment modality utilized for managing axial or discogenic pain, including epidural injections. In an interventional pain management practice in the US, a randomized, double-blind, active control trial was conducted. The objective was to assess the effectiveness of lumbar interlaminar epidural injections of local anesthetic with or without steroids for managing chronic low back pain of discogenic origin. However, disc herniation, radiculitis, facet joint pain, or sacroiliac joint pain were excluded. Two groups of patients were studied, with 60 patients in each group receiving either local anesthetic only or local anesthetic mixed with non-particulate betamethasone. Primary outcome measures included the pain relief-assessed by numeric rating scale of pain and functional status assessed by the, Oswestry Disability Index, Secondary outcome measurements included employment status, and opioid intake. Significant improvement or success was defined as at least a 50% decrease in pain and disability. Significant improvement was seen in 77% of the patients in Group I and 67% of the patients in Group II. In the successful groups (those with at least 3 weeks of relief with the first two procedures), the improvement was 84% in Group I and 71% in Group II. For those with chronic function-limiting low back pain refractory to conservative management, it is concluded that lumbar interlaminar epidural injections of local anesthetic with or without steroids may be an effective modality for managing chronic axial or discogenic pain. This treatment appears to be effective for those who have had facet joints as well as sacroiliac joints eliminated as the pain source.

Keywords: lumbar disc herniation, axial or discogenic pain, lumbar interlaminar epidural injections, local anesthetic, steroids, controlled comparative local anesthetic blocks, NCT00681447

Introduction

Epidural injections are one of the most commonly utilized treatment modalities for managing chronic low back pain with or without lower extremity pain.¹⁻¹² Despite increasing utilization of lumbar epidural injections, significant debate continues regarding their effectiveness, specifically any conditions other than disc herniation and compressive radiculitis. The pathophysiology of low back pain and radicular pain is the subject of ongoing research and controversy, with discogenic pain assuming a major role as a cause of non-specific low back pain, beyond disc herniation.¹³⁻¹⁶ In fact, soon after the description of intervertebral disc herniation by Mixter and Barr¹⁷ in American medical literature in 1934 with their landmark description of the herniated nucleus pulposus,
Mixer and Ayers showed that radicular pain can occur without disc herniation. Further, non-specific low back pain constitutes 80% or 90% of low back pain without identifiable causes with a large proportion having chronic axial low back pain secondary to progressive degenerative disc disease. It has been shown that discs have innervation with deep ingrowth into degenerated intervertebral discs. Animal models have identified upregulation of various molecules such as calcitonin gene-related peptide and substance P in dorsal root ganglion neurons innervating degenerated intervertebral discs. Research also has detected high levels of inflammatory mediators in degenerated discs. While the majority of patients with axial low back pain improve with conservative management, various types of interventions have been described for chronic patients, but most interventions are highly variable and are associated with poor outcomes.

In the past, all axial pain was attributed to disc degeneration. However, the development of controlled diagnostic blocks, and interventional techniques including discography, facet joint blocks, and sacroiliac joint blocks, have provided evidence that axial pain can also be caused by facet joints and sacroiliac joints. Utilizing provocation discography, the prevalence of pain due to internal disc disruption was reported to be 39% in patients suffering with chronic low back pain, whereas primary discogenic pain was reported in 26% when no other cause was suspected. In addition, facet joint pain has been shown to be present in 21%-41% of patients, whereas sacroiliac joint pain has been established in 10%-38% of a selected population.

The underlying mechanism of action for epidurally administered local anesthetic and steroids has been described, though not well understood. However, historically it has been believed that epidural steroids function by reducing inflammation, thus limiting the indications to compressive radiculopathy or, at best, radiculitis secondary to chemical irritation. Much of the literature on lumbar interlaminar epidurals has been negative except in recent years when fluoroscopic guidance was utilized. A variation of lumbar interlaminar injections, caudal epidural injections, have also been proven to be effective in multiple causes of low back pain with or without lower extremity pain. Recent evidence also has demonstrated effectiveness for fluoroscopically administered epidural injections in the cervical spine as well as the thoracic spine. These evaluations have illustrated the effectiveness of epidural injections not only for disc herniation, but also for axial or discogenic pain after eliminating facet and sacroiliac joint pain, spinal stenosis, and post-surgery syndrome. In fact, in the published preliminary results of the current study, lumbar interlaminar epidural injections provided improvement in 74% of patients who received local anesthetic only, and 63% in the group who received local anesthetic and steroids.

The current report evaluates the role of lumbar interlaminar epidural injections for patients with chronic axial or discogenic low back pain in 120 patients with a 1-year follow-up.

**Methods**

This active control, randomized, double-blind trial was conducted in an interventional pain management practice, in a specialty referral center, with approval of the Institutional Review Board (IRB). It follows Consolidated Standards of Reporting Trials (CONSORT) guidelines. The study is registered with the US Clinical Trial Registry with an assigned number of NCT00681447.

The internal resources of the practice were used to conduct the study. There was no external funding, either from industry or from elsewhere.

**Interventions**

Patients were assigned into one of two groups. Group I patients received lumbar interlaminar epidural injections with 6 mL of lidocaine 0.5% preservative free; Group II patients received lumbar interlaminar epidural injections with 5 mL of lidocaine 0.5% preservative-free mixed with 6 mg or 1 mL of non-particulate betamethasone.

**Participants**

All patients were recruited from new patients presenting to the center who met the inclusion criteria. The IRB-approved protocol and informed consent, which described in detail all aspects of the study and its process, were provided to all participating patients.

**Pre-enrollment data collection**

The data collected included Numeric Rating Scale (NRS) for pain, Oswestry Disability Index 2.0 (ODI) for functional status, medical and surgical history of any co-existing disease(s), radiologic investigations, physical examination, work status, and opioid intake.

**Inclusion criteria**

Inclusion criteria included only the patients with a diagnosis of lumbar axial or discogenic pain; over the age of 18 years; a history of chronic function-limiting low back pain of at least 6 months duration; and the ability to understand the study protocol and provide voluntary, written informed consent, and participate in outcome measurements.
Additional criteria were a failure to improve with conservative management, including, but not limited to, physical therapy, chiropractic manipulation, exercises, drug therapy, and bedrest.

Exclusion criteria were a positive response for lumbar facet joint or sacroiliac joint pain by means of controlled, comparative local anesthetic blocks; previous lumbar surgery; uncontrollable or unstable opioid use; uncontrollable psychiatric disorders; uncontrollable medical illness, either acute or chronic; any conditions that could interfere with the interpretation of the outcome assessments; pregnant or lactating women; and a history or potential for adverse reaction(s) to local anesthetics or steroids.

Description of interventions
All participating patients were evaluated with controlled, comparative local anesthetic lumbar facet joint nerve blocks or sacroiliac joint injections. The process started with diagnostic facet joint nerve blocks with 0.5 mL of 1% lidocaine, followed by the blockade of facet joint nerves with 0.25% bupivacaine on separate occasions. A positive response was 80% pain relief. Controlled, comparative local anesthetic blocks were also performed for suspected sacroiliac joint pain, with 2 mL of 1% lidocaine and 0.25% bupivacaine.

Lumbar interlaminar epidural procedures were performed by one physician (LM) in an ambulatory surgery setting, in sterile operating room, utilizing fluoroscopy. Patients were in the prone position with intravenous access and sedation as indicated. The epidural space entry was confirmed by an injection of non-ionic contrast medium. All procedures were performed either between L5 and S1 or at a higher level based on the patient’s pain complaints. Following this, an injection of 6 mL of lidocaine hydrochloride 0.5% preservative-free, or 5 mL of lidocaine mixed with 6 mg of non-particulate betamethasone was given. The opioid intake was converted into morphine equivalents.

Additional interventions
If a patient required additional lumbar interlaminar epidural injections, these were provided based on the response to the previous injection, with deterioration of pain relief to less than 50%. Patients who were non-responsive and continued with conservative management were followed without further epidural injections with medical management, unless they requested unblinding.

Co-interventions
There was no specific physical therapy, occupational therapy, bracing, or other interventions offered other than the study intervention. In addition, if patients were improving significantly and the medical necessity for drugs was lacking, medications were stopped or dosages were decreased. For some patients, based on medical necessity, dosages were increased. However, all patients continued previously directed exercise programs, as well as their employment.

Objective
The study was designed to assess the effectiveness of lumbar interlaminar epidural injections containing local anesthetic with or without steroids in managing chronic axial low back pain of discogenic origin.

Outcomes
Primary outcome measures included the NRS on a scale of 0–10, and the ODI on a 0–50 scale. Secondary outcome measures included employment status, and opioid intake in terms of morphine equivalents. The value and validity of the NRS and ODI have been reported. Recently, previously established thresholds were questioned. Thus, significant pain relief or improvement and function were considered to be at least a 50% reduction in NRS and the ODI, which is similar to the measurements in other trials.

The opioid intake was considered to be successful if a patient obtained significant improvement for at least 3 weeks with the first and second procedures. All others were considered to be failures.

Sample size
The sample size was calculated based on significant pain relief. Considering a 0.05 two-sided significance level, a power of 80%, and an allocation ratio of 1:1, 55 patients in each group were estimated. Allowing for a 10% attrition/ non-compliance rate, 60 patients were required.

Randomization
Sixty patients were randomly assigned into each group from a total of 120 patients who met inclusion criteria.
Sequence generation
Simple randomization was utilized to allocate patients into groups.

Allocation concealment
Patients were randomized into two groups by one of the three operating room nurses who were also study coordinators. The same person also prepared the drugs.

Blinding (masking)
The patients and physician were blinded to group assignment and both injectates were clear. In addition, the blinding was ensured by mixing the study patients with other patients receiving routine treatment. All patients chosen for 1-year follow-up were selected by a statistician not participating in provision of the patients’ care and the unblinding results were not disclosed to either the treating physician, other participants, or patients. Thus, the nature of blinding was not interrupted.

Statistical methods
Data analyses were carried out using SPSS software (v 9.01; SPSS Inc, Chicago, IL). For categorical and continuous data comparison, Chi-square (Fisher test where necessary) and t-tests were used, respectively. Because the outcome measures of the participants were measured at four points in time, repeated measures analysis of variance were performed with the post hoc analysis.

Intent-to-treat analysis
Either the last follow-up data or initial data were utilized in the patients who dropped out of the study and no other data were available for the intent-to-treat analysis.

Best case, worst case, and last follow-up score scenarios were used for sensitivity analysis.

Results
Participant flow
Figure 1 illustrates the participant flow. The recruitment period lasted from January 2008 through May 2010.

Baseline data
Table 1 shows the basic demographic characteristics, pain distribution, onset of the pain, numeric rating scale of pain, and ODI for functional status summary scores. There were no statistically significant differences between the two groups in terms of these baseline data (all \( P \) values > 0.05), except for weight (\( P = 0.000 \)).

Pain relief and functional assessment
Table 2 presents the results of repeated measures analysis. Regarding pain scores, there were significant differences within groups by time (\( P = 0.001 \)). In the ODI for functional status, there were significant differences in summary scores within group by time (\( P = 0.001 \)).

A post hoc analysis indicated that all the mean differences between baseline and with the scores at other time points were significant at the 0.05 level.

Pain relief and functional status improvement
The percentage of patients with significant improvement is presented in Figure 2. In Group I and II, 77% and 67% showed significant improvement, respectively. In the successful groups, significant improvement was seen in 84% in Group I and 71% in Group II.

Therapeutic procedural characteristics
Table 3 lists therapeutic procedural characteristics. Lumbar interlaminar procedures were performed in 91% of cases at L5/S1 and 9% of cases at L4/5.

Employment characteristics
Table 4 lists employment characteristics in both groups. Among the patients eligible for employment, the total employed changed from 12 at baseline to 13 at the end of 12 months in Group I; it changed from 14 to 18 in Group II, a nonsignificant increase of 6% in Group I and 21% in Group II.

Opioid intake
Table 5 presents the results of repeated measures analysis for opioid intake. There were significant differences in opioid intake within group by time (\( P < 0.001 \)). A post hoc analysis indicated that all the mean differences in scores between baseline and other time points were significant at the 0.05 level.

Changes in weight
Table 6 shows changes in weight, with no significant differences in changes among the groups.

Adverse events
Of the 454 lumbar epidural procedures performed, there were two subarachnoid punctures that did not result in headache. One patient experienced weight gain due to a high dose of steroid from an unrelated medical problem.
This randomized, active control trial shows that carefully selected patients with axial or discogenic chronic low back pain can receive significant pain relief and functional status improvement with lumbar interlaminar epidural injections. Their pain was not caused by disc herniation, facet joints, or the sacroiliac joints. Significant pain relief and functional status improvement of ≥50% were seen in 77% of Group I and 67% of Group II. A better picture emerges when each group was divided into failed and successful outcomes. Significant pain relief and functional status improvement was seen in 84% of the successful outcomes in Group I; 71% in the successful outcomes in Group II. The average procedures per year and average weeks of total relief for the successful outcome patients were: Group I, 3.9 procedures and 40.0 ± 15.6 weeks; Group II, 4.0 procedures and 39.6 ± 12.4 weeks.
Table 1 Baseline demographic and clinical data

<table>
<thead>
<tr>
<th></th>
<th>Group I (60)</th>
<th>Group II (60)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>23% (14)</td>
<td>40% (24)</td>
<td>0.077</td>
</tr>
<tr>
<td>Female</td>
<td>77% (46)</td>
<td>60% (36)</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>41.2 ± 11.9</td>
<td>42.7 ± 11.4</td>
<td>0.477</td>
</tr>
<tr>
<td>Weight</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>211.2 ± 60.9</td>
<td>168.6 ± 40.6</td>
<td>0.000</td>
</tr>
<tr>
<td>Height</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>65.8 ± 3.7</td>
<td>66.4 ± 4.1</td>
<td>0.430</td>
</tr>
<tr>
<td>Duration of pain (months)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>104.2 ± 106.5</td>
<td>129.0 ± 90.9</td>
<td>0.173</td>
</tr>
</tbody>
</table>

The results of this evaluation essentially illustrate that if patients are selected appropriately, lumbar epidural injections provide significant improvement. These results are in line with other studies separating the patients into failed and successful groups.

Table 2 Comparison of numeric rating scale for pain and Oswestry disability index score summaries at four time points

<table>
<thead>
<tr>
<th>Time points</th>
<th>Numeric pain rating scale</th>
<th>Oswestry disability index</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group I (60)</td>
<td>Group II (60)</td>
</tr>
<tr>
<td></td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>Baseline</td>
<td>8.0 ± 1.0</td>
<td>7.7 ± 0.9</td>
</tr>
<tr>
<td>3 months</td>
<td>3.6* ± 0.9</td>
<td>3.5* ± 1.2</td>
</tr>
<tr>
<td>6 months</td>
<td>3.9* ± 1.1</td>
<td>3.6* ± 1.2</td>
</tr>
<tr>
<td>12 months</td>
<td>3.7* ± 1.2</td>
<td>3.7* ± 1.3</td>
</tr>
</tbody>
</table>

Group difference 0.208  0.395
Time difference 0.001  0.001
Group by time interaction 0.448  0.210

Notes: Lower the value, the better the condition; *Significant difference with baseline values within the group (P < 0.05); ( ) illustrates proportion with significant pain relief (≥50%) from baseline.
Epidural injections in axial low back pain

3.8
10.2
36.8
Combined
40.0
11.6
3.9
11.9
2.2
12.6
12.2
6.1
2.0
11.9
12.0
1.6
39.6
Group II
0.9
8.2
–
36.0
12.1
10.1
4.0
Successful patients
3.5
1.6
3.7
2.0
12.6
3.2
Figure 2 Percentage of patients with a significant reduction in Numeric Rating Score and Oswestry disability index (≥50% reduction from baseline).

limentary version of this study.39 Buttermann51 evaluated the role of interlaminar epidural steroids showing improvement only at the 3-month follow-up. All of the studies reported modest results.

The mechanism of action of steroids and local anesthetics continues to be debated. Multiple hypothesis have been emerging.76–84 The evidence shows that steroids, as well as local anesthetics, have significant effects on the modulation of noxious stimulation by various mechanisms. Long-term effects are provided by both local anesthetics and steroids or when in combination, in experimental as well as clinical studies.38,46,47,54–56,58–61,76–84

Comparative effectiveness research and evidence-based medicine have been considered as pivotal to health care policy not only in the US, but across the world.10,11,85–89 In general, practical studies conducted in a generally applicable environment are considered more valuable than pragmatic or practical clinical trials with an active control group instead of a placebo group. Practical studies measure effectiveness, which is considered more appropriate than explanatory trials which measure efficacy.90–93 Thus, this study meets the criteria for a practical clinical trial, specifically in contemporary interventional pain management practices; it meets the appropriate selection criteria and repeats the procedures based upon the return of pain, rather than a predetermined schedule. The procedures were performed under fluoroscopy, only after conservative management had failed. The study also confirms the long-held belief that if the first two procedures do not provide at least a minimum of 3 weeks of relief, the procedures may not provide relief on a long-term basis. This was observed in the failed patients, suggesting that it may be futile to continue to repeat these procedures in these patients, unless there are compelling reasons to do so.

Table 3 Therapeutic procedural characteristics with procedural frequency, average relief per procedure, and average total relief in weeks over a period of 1 year

<table>
<thead>
<tr>
<th>Average relief</th>
<th>Successful patients</th>
<th>Failed patients</th>
<th>Combined</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group I (55)</td>
<td>Group II (54)</td>
<td>Group I (5)</td>
</tr>
<tr>
<td>1st procedure relief</td>
<td>6.1 ± 3.8 (55)</td>
<td>6.5 ± 4.3 (54)</td>
<td>0.9 ± 1.0 (5)</td>
</tr>
<tr>
<td>2nd procedure relief</td>
<td>10.2 ± 6.8 (55)</td>
<td>10.0 ± 6.7 (54)</td>
<td>1.0 ± 1.4 (2)</td>
</tr>
<tr>
<td>3rd procedure relief</td>
<td>11.9 ± 4.1 (51)</td>
<td>11.0 ± 3.5 (50)</td>
<td>2.0 ± 1.0 (1)</td>
</tr>
<tr>
<td>4th procedure relief</td>
<td>12.2 ± 4.5 (38)</td>
<td>12.3 ± 2.3 (41)</td>
<td>–</td>
</tr>
<tr>
<td>5th procedure relief</td>
<td>12.6 ± 1.1 (16)</td>
<td>13.3 ± 2.7 (18)</td>
<td>–</td>
</tr>
<tr>
<td>Number of procedures per year</td>
<td>3.9 ± 0.9 (16)</td>
<td>4.0 ± 0.9 (18)</td>
<td>1.6 ± 0.9 (8)</td>
</tr>
<tr>
<td>For initial 2 procedures in weeks</td>
<td>8.6 ± 10.0 (215)</td>
<td>8.2 ± 5.9 (218)</td>
<td>0.9 ± 1.0 (8)</td>
</tr>
<tr>
<td>After initial 2 procedures</td>
<td>12.1 ± 3.9 (215)</td>
<td>11.9 ± 3.1 (218)</td>
<td>2.0</td>
</tr>
<tr>
<td>All procedures</td>
<td>10.1 ± 5.4 (215)</td>
<td>10.1 ± 5.0 (218)</td>
<td>1.1 ± 1.0 (8)</td>
</tr>
<tr>
<td>Total relief per year (weeks)</td>
<td>40.0 ± 15.6 (396 ± 12.4)</td>
<td>39.6 ± 12.4 (396 ± 12.4)</td>
<td>1.6 ± 1.7 (32 ± 5.4)</td>
</tr>
</tbody>
</table>

Note: Successful groups had at least 3 weeks of relief with first two procedures.
Table 4 Employment characteristics

<table>
<thead>
<tr>
<th>Employment status</th>
<th>Group I Baseline</th>
<th>Group I 12 months</th>
<th>Group II Baseline</th>
<th>Group II 12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Employed part-time</td>
<td>7</td>
<td>5</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Employed full-time</td>
<td>5</td>
<td>8</td>
<td>11</td>
<td>13</td>
</tr>
<tr>
<td>Unemployed (due to pain)</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Not working</td>
<td>3</td>
<td>4</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Eligible for employment</td>
<td>17</td>
<td>17</td>
<td>19</td>
<td>19</td>
</tr>
<tr>
<td>Total employed</td>
<td>12</td>
<td>13</td>
<td>14</td>
<td>18</td>
</tr>
<tr>
<td>Housewife</td>
<td>3</td>
<td>3</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Disabled</td>
<td>39</td>
<td>38</td>
<td>32</td>
<td>32</td>
</tr>
<tr>
<td>Retired/over 65</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Total number of patients</td>
<td>60</td>
<td>60</td>
<td>60</td>
<td>60</td>
</tr>
</tbody>
</table>

The present study may be criticized for not focusing on a placebo group. However, most studies have utilized inappropriate methodology with placebo groups with reference to interventional techniques. The only appropriately designed placebo trial by Ghahreman et al showed a lack of significant effect when sodium chloride solution was injected into an inactive structure. Consequently, when sodium chloride solution or other agents such as local anesthetics, which are considered as placebo by some do not yield the same results, this leads to inaccurate methodology and conclusions.

Some of the other weaknesses include differences in baseline demographic characteristics with respect to weight and sex; however, these differences were not considered to have caused any significant effect on the final results.

The implications of this trial are enormous in the health care arena. Studies with proper methodology in practical settings are not only crucial, but mandatory. Proper application of interventions will improve not only patients’ pain and function and reduce drug use, it may also return them to the workforce; however, by the same token, inappropriate provision of any type of intervention, specifically interventions with substantial expenses, will not provide any benefit. Instead, it can harm the patient, thus depleting resources and reducing access. Similarly, inappropriately performed evaluations in the name of methodology, leading to inaccurate conclusions, may reduce health care expenditures, and will also increase patient suffering and reduce function by impeding access to much needed medical care.

Conclusion

This study illustrates that overall significant improvement was seen in 77% of the patients in Group I and 67% of the patients in Group II. In the successful outcome groups, in those who received at least 3 weeks of relief with the first two procedures, the improvement was 84% in Group I and 71% in Group II. Pain relief and functional status improvement was achieved with an average procedures per year in the successful outcome groups of 3.9 in Group I and 4.0 in Group II, and an average total relief per year of 40.0 ± 15.6 weeks in Group I and 39.6 ± 12.4 in Group II.

Acknowledgments/ethics approval

Dr Manchikanti and Dr Benyamin designed the study; Mr Pampati performed the statistical analysis, and Ms Cash and Ms McManus were two of the three coordinators. The study was approved by the IRB and was registered in the US Clinical Trial Registry. All ethical guidelines were followed.

Disclosure

The authors report no conflicts of interest in this work.

References

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