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Randomized Trial

A Randomized, Double-Blind, Active-Controlled Trial of Fluoroscopic Lumbar Interlaminar Epidural Injections in Chronic Axial or Discogenic Low Back Pain: Results of 2-Year Follow-Up

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Background: Chronic low back with or without lower extremity pain is extremely common, expensive, and disabling. Although it is responsible for a very small proportion of patients, disc herniation is the primary focus of modalities of treatments. In fact, chronic low back pain without disc herniation is common. Multiple modalities of treatments are utilized in managing axial or discogenic pain without disc herniation including surgery, intradiscal therapies, and epidural injections. There is, however, continued debate on the effectiveness, indications, and medical necessity of all modalities of treatments in managing axial or discogenic pain in the lumbar spine.

Objectives: To assess the effectiveness of lumbar interlaminar epidural injections in managing chronic axial or discogenic low back pain with epidural injections of local anesthetic with or without steroids.

Study Design: A randomized, double-blind, active-controlled trial.

Setting: A private practice, specialty referral, interventional pain management practice in the United States.

Methods: In this study, a total of 120 patients were randomly allocated to one of 2 groups of 60 patients receiving either local anesthetic alone or local anesthetic with steroids. The primary outcome measure was at least a 50% improvement in the numeric rating scale (NRS) and Oswestry Disability Index (ODI). Outcomes were assessed at 3, 6, 12, 18, and 24 months post treatment.

Results: Significant pain relief and functional status improvement, defined as a reduction in scores from baseline of at least 50% or more, were observed in 72% of patients receiving local anesthetic alone and 67% of patients receiving local anesthetic with steroids. Opioid intake was reduced from the baseline in each group for 2 years.

Limitations: The results of the study are limited by the lack of a placebo group.

Conclusion: Lumbar interlaminar epidural injections of local anesthetic with or without steroids are effective in patients with chronic axial low back pain of discogenic origin without facet joint pain, disc herniation, and/or radiculitis.

Key words: Lumbar disc herniation, axial or discogenic pain, lumbar interlaminar epidural injections, local anesthetic, steroids, controlled comparative local anesthetic blocks

Trial Registration: NCT00681447

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Chronic low back pain has become a major disabling condition in the US, with increasing prevalence as well as social and economic impact (1-8). In fact, the state of US Health, from 1999 to 2010 assessing risk factors as well as the burden of disease and injuries, shows low back pain to be the number one cause of disability in US (1). Accurate cause of low back pain is determined in a very small proportion of patients, with the disc herniation contributing to a minute Proportion, which can be readily identified and managed with proven therapies (8-14). Consequently, discogenic pain arising from the disc itself without disc herniation, radiculitis, facet joint pain, or sacroiliac joint pain has been described as axial, nonradicular, chronic low back pain in the absence of spinal deformity, instability, and signs of nerve root irritation (8-19). Thus, in the absence of evidence of disc herniation, localization of the painful disc based on the symptoms and signs elicited on physical examination may be extremely difficult. Axial low back pain without radiculitis is similar to the pain produced by zygapophysial joints, the sacroiliac joint, or musculoligamentous origin of pain (8-14). Consequently, it is widely believed that lumbar disc herniation is not the major cause of low back pain, and that discogenic pain caused by annular disruption is one of the most important causes of chronic axial low back pain (14,17).

Intervertebral disc degeneration is an age-related process that is asymptomatic in most individuals. Pathologic degeneration, however, can be a major cause of pain and disability (14,17). At present, the term "discogenic low back pain" refers specifically to the pain caused by internal disc disruption (IDD) as described by Crock (18). Crock (18) proposed the concept of IDD as a condition marked by alteration in the internal structure and metabolic functions of the intervertebral disc. IDD is often thought of as being related annular injury and subsequent repair of the annulus fibrosis (2). Singh et al (19) classified discogenic low back pain as a separate clinical entity to be differentiated from other types of disc degenerative diseases, such as lumbar disc herniation, lumbar spinal stenosis, and lumbar segmental instability. Utilizing controlled diagnostic blocks, the prevalence of pain due to IDD was reported to be 39% and 42% in patients suffering from chronic low back pain (9,12), whereas primary discogenic pain was reported in 26% when no other cause was suspected (11). It should be noted that these results are based on the accuracy of lumbar provocation discography. Peng et al (14) assessed the natural history of discogenic low back pain over4 years of follow-up. A total of 156 patients or 56% were diagnosed with discogenic low back pain based on lumbar discography and the International Association for the Study of Pain criteria for IDD. At the 4-year follow-up with a follow-up rate of 84%, only 13% had their low back pain symptoms alleviated and lumbar function improved; 7.6% slightly improved; 12.2% had their symptoms aggravated; and 67.2% experienced the same pain and disability as before.

The normal intervertebral disc is avascular and aneural, except for the outer third of the annulus fibrosis which is innervated by sensory nerve endings from the dorsal root ganglia (DRG) (20-22). However, as the disc degeneration advances, disc inflammation may promote axonal growth of afferent fibers innervating the disc by secreting proinflammatory mediators, such as tumor necrosis factor and interleukin-6 (23). In addition, trophic growth factor for sympathetic and sensory nerve cells – nerve growth factor (NGF) stimulates the differentiation, growth, maintenance, and survival of sympathetic and sensory nerve cells (24). Thus, pain signals could be triggered as the neurons of the DRG transmit the inflammatory signal through the spinal cord to the pain centers of the brain (21,25). Furthermore, recent studies have also revealed that NGF shows hyperalgesic properties by sensitizing and sprouting sensory nerve fibers in painful pathological conditions (20,26,27). Thus, it has been proposed that the actions of NGF in painful intervertebral disc tissue not only sensitize the sensory nerves, but also stimulate the peripheral nociceptive sensory neurons to grow into the intervertebral disc tissue where in most cases the extracellular matrix has degenerated (28-31). Consequently, relieving the inflammatory tension of the DRG or regulating the NGF is accomplished by utilizing nonsteroidal antiinflammatory drugs, epidural steroid injections, and various other drugs.

The diagnosis of discogenic pain (32,33) does not have well established criteria. Thus, multiple modalities of treatments have been offered to eliminate the pain source by surgical excision, fusion, or artificial disc replacement and occasionally with nonsurgical treatment (32,33). Based on randomized trials comparing fusion with nonsurgical care, however, lumbar spinal fusion has been proven to have only a minimal effect (33-38). In addition, artificial disc studies showed disc replacement to have less than a 60% success rate for a composite outcome and even lower success for comparator lumbar fusion in studies submitted to the Food

and Drug Administration for investigational device exemption (39-41). A Cochrane Review of 7 randomized trials showed only mild improvement (42). Independent evidence reviews by the Centers for Medicare and Medicaid Services Coverage and Advisory Committee (43) and the Washington Health Care Technology Assessment Program (44) concluded that lumbar fusion for degenerative disc disease lacks sufficient evidence of efficacy and safety to justify continued coverage. Furthermore, evidence from conservative management, including physical therapy or other rehabilitation modalities as well as intradiscal therapy and medical therapy has been limited (8,45-50).

As an alternative to surgical fusion or intradiscal therapies, Manchikanti et al (15,16,51-55) have proposed managing patients with axial or discogenic pain, diagnosed by performing or not performing provocation discography, with epidural injections after appropriately eliminating the facet joint, as well as eliminating sacroiliac joint causation by using controlled diagnostic blocks. Furthermore, systematic reviews and guidelines have shown fair evidence for treating axial low back or discogenic pain with caudal and lumbar interlaminar epidural injections, whereas the evidence was poor for transforaminal epidural injections (8). In fact, Manchikanti et al (15), in assessing the efficacy of fluoroscopic caudal epidural injections in managing chronic axial low back pain without disc herniation, radiculitis, or facet joint pain in 120 patients. They reported significant overall improvement (defined as a 50% or more reduction in pain scores from baseline), along with improvement in functional status. They reported 54% or 60% improvement at 24 months in the groups receiving local anesthetic with or without steroids, whereas in the successful group, 84% of the patients who received local anesthetic only and 73% of the patients who received local anesthetic and steroids showed significant pain relief and functional status improvement in the successful groups at 24 months. Successful groups were considered those with at least 3 weeks of improvement with the first 2 procedures. In a one-year follow-up of lumbar interlaminar epidural injections in managing chronic lumbar axial or discogenic pain, Manchikanti et al (16) showed 77% and 67% overall improvement in patients with local anesthetic only, or with local anesthetic and steroids, and 84% and 71% in the successful group.

In addition, these results are comparable to the results of injections with or without steroids for disc herniation, lumbar postsurgery syndrome, and central spinal stenosis (8).Consequently, this study sought to evaluate the role of lumbar interlaminar epidural injections in patients with chronic low back pain without disc herniation, radiculitis, facet joint pain, sacroiliac joint pain, or other sources of chronic low back pain. Patients were shown to be negative for facet joint and sacroiliac joint pain by controlled, comparative local anesthetic blocks. This report is the final report of 120 patients at 2-year follow-up; one year results were previously published (16).

Methods

This active control, randomized, double-blind trial of lumbar interlaminar epidural injections with or without local anesthetic was conducted based on Consolidated Standards of Reporting Trials (CONSORT) guidelines (56,57). The study was performed in a specialty referral center and was reviewed by the Institutional Review Board (IRB). The study was also registered with the US Clinical Trial Registry with an assigned number of NCT00681447.

No external resources were utilized in the conduct of this study.

Participants

All participants in the study were identified from the new patient pool of the practice. Eligible patients were provided with the IRB-approved protocol and informed consent describing in detail all aspects of the study.

Interventions

One hundred and twenty patients were assigned into 2 groups with 60 patients in each group. Group I patients were assigned to receive lumbar interlaminar epidural injections with 0.5% preservative-free lidocaine 6 mL, whereas, Group II patients were assigned to receive lumbar interlaminar epidural injections with a total volume of 6 mL derived from preservative-free lidocaine 0.5%, 5 mL, mixed with 1 mL of 6 mg non-particulate betamethasone.

Pre-enrollment Data Collection

Comprehensive data collection occurred prior to enrollment. This included outcome parameters collected using the Numeric Rating Scale (NRS) for pain and Oswestry Disability Index 2.0 (ODI) to determine the functional status, as well as medical and surgical history of coexisting disease(s), radiological investigations, physical examination, work status, and opioid intake.

Inclusion Criteria

Only patients with lumbar axial or discogenic pain were included. Patients were required to be over the age of 18 years with 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. In addition, all the patients should have undergone controlled comparative local anesthetic blocks to rule out either facet joint pain or sacroiliac joint pain if suspected, and failed to improve significantly with conservative management, including various rehabilitation modalities such as physical therapy, chiropractic manipulation, structured exercise program, and other modalities including behavioral therapy, drug therapy, and bedrest.

Exclusion criteria included the presence of facet joint pain or sacroiliac joint pain, previous lumbar surgery, opioid use which was uncontrolled or unstable, psychiatric disorders which were not controlled, uncontrolled medical illness (either acute or chronic), and any conditions that could interfere with the interpretation of the outcome assessments. Pregnant or lactating women and those with a history of potential for adverse reaction(s) to local anesthetics or steroids were also excluded.

Description of Interventions

Controlled comparative local anesthetic lumbar facet joint nerve blocks or sacroiliac joint injections were administered to all patients prior to enrolling in this trial. The process of eliminating facet joint pain when suspected began with diagnostic facet joint nerve blocks with 0.5 mL of 1% lidocaine, followed by facet joint nerve blocks with 0.25% bupivacaine. Pain relief of 80% was considered a positive response (8,11,12,58,59). Controlled, comparative local anesthetic blocks of 2 mL of 1% lidocaine and 0.25% bupivacaine were also performed for suspected sacroiliac joint pain (8,11,12,58,59).

In a sterile operating room, utilizing fluoroscopy, one physician (LM) performed the lumbar interlaminar epidural procedures. All patients were positioned in a prone position with intravenous access and were sedated as indicated. Nonionic contrast was injected to confirm epidural space entry. All procedures were performed between L5 and S1 or at a higher level based on the patient's pain. Following the injection of nonionic contrast medium, 6 mL of lidocaine hydrochloride 0.5% preservative-free, or 5 mL of lidocaine mixed with 6 mg of nonparticulate betamethasone was injected.

Additional Interventions

Additional lumbar interlaminar epidural injections were performed only if the patient's response resulted in deterioration of pain relief and functional status of less than 50%; however, patients who were nonresponsive were also continued with conservative management and were followed without further epidural injections with medical management. Any patient who requested to be removed from the study was unblinded.

Co-Interventions

Co-interventions were similar in both groups. These included the continuation of previously directed structured exercise programs, employment, and medical therapy. There was no one specific type of intervention in any of the patients including physical therapy or other interventions.

Objective

The objective of this trial was 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

Multiple outcome measures included the NRS on a scale of 0 – 10, the ODI on a 0 – 50 scale, employment status, and opioid intake in terms of morphine equivalents. The value and validity of the NRS and ODI have been documented (60-62).

Significant pain relief or improvement were considered to be at least a 50% reduction in the NRS and ODI, which is a robust measure and extends beyond the recommended minimum changes utilized in a multitude of studies (63-66).

Opioid intake was converted into morphine equivalents (67).

For assessment of employment and work status, patients were classified into multiple categories such as employable, housewife with no desire to work outside the home, retired, or over the age of 65. Patients who were unemployed due to pain, employed but on sick leave, or laid off were considered to be employable.

A successful response was considered as at least 3 weeks of relief with the first and second procedures,

whereas all other responses were considered as failures.

Outcomes were assessed at 3, 6, 12, 18, and 24 months in both groups.

Sample Size

Fifty-five patients in each group were estimated based on significant pain relief, for a 0.05 2-sided significance level, a power of 80%, and an allocation ratio of 1:1 (68). However, with a 10% attrition/non-compliance rate, the required sample size was 60 patients in each group (68).

Randomization

A total of 120 patients were selected for randomization. Of these, 60 patients were randomly assigned into each group.

Sequence Generation

Sequence generation for randomization of the 120 patients was based on a computer-generated random allocation sequence by simple randomization.

Allocation Concealment

To maintain allocation concealment, randomization was performed based on sequence generation by one of the 3 trial coordinators. The person randomizing the patients also prepared the drugs.

Blinding (Masking)

To maintain proper blinding the physician, patient, and all others were blinded to group assignment. In addition, injectates in both groups were clear and similar. Blinding was also maintained by mixing the trial patients with other patients receiving routine treatment. The nature of the blinding was not interrupted at any stage.

Statistical Methods

For categorical and continuous data comparison, Chi-square (Fisher's exact test where necessary) and t test were used respectively. Because the outcome measures of the patients were measured at 6 points in time, repeated measures analysis of variance were performed with the post hoc analysis. Data analyses were carried out using the Statistical Package for Social Sciences version 9.01 (SPSS Inc, Chicago, IL).

Intent-to-Treat Analysis

Best case, worst case, and last follow-up score scenarios were used for sensitivity analysis. Either the last follow-up data or initial data were utilized in patients who dropped out of the study and for whom no other data were available for the intent-to-treat analysis.

Results

Participant Flow

The recruitment was from January 2008 through May 2010. Figure 1 illustrates the participant flow.

Baseline Data

Baseline demographics and clinical characteristics are shown in Table 1. While all characteristics were similar, patients in Group I weighed more than patients in Group II.

Pain Relief and Functional Assessment

Table 2 shows the comparison of numeric pain rating scale and ODI score summaries, the with results based on repeated measures analysis. There were significant differences from baseline to 24 months in both parameters; however, there were no significant differences between the groups.

Figure 2 illustrates significant improvement in successful patients, failed patients, and all patients with 78% and 70% showing improvement in the successful group and 72% and 67% showing improvement when all patients are considered.

Therapeutic Procedural Characteristics

Lumbar interlaminar procedures were performed in 90% of the patients between L5 and S1, and 10% of the patients between L4 and L5. Therapeutic procedural characteristics are shown in Table 3. This table also shows an average number of procedures of approximately 6 for both groups for 2 years and relief for the initial 2 procedures lasting approximately 8 weeks. An overall average relief per procedure of 12 weeks, along with an average total relief for 2 years of 73.2 ± 29.3 weeks was seen in the successful group in Group I and 71.2 ± 29.4 in the successful group in Group II. Among all patients, overall total relief was 67.3 ± 34.6 weeks in Group I and 64.4 ± 34.7 weeks in Group II.

Employment Characteristics

Table 4 lists employment characteristics in both groups.

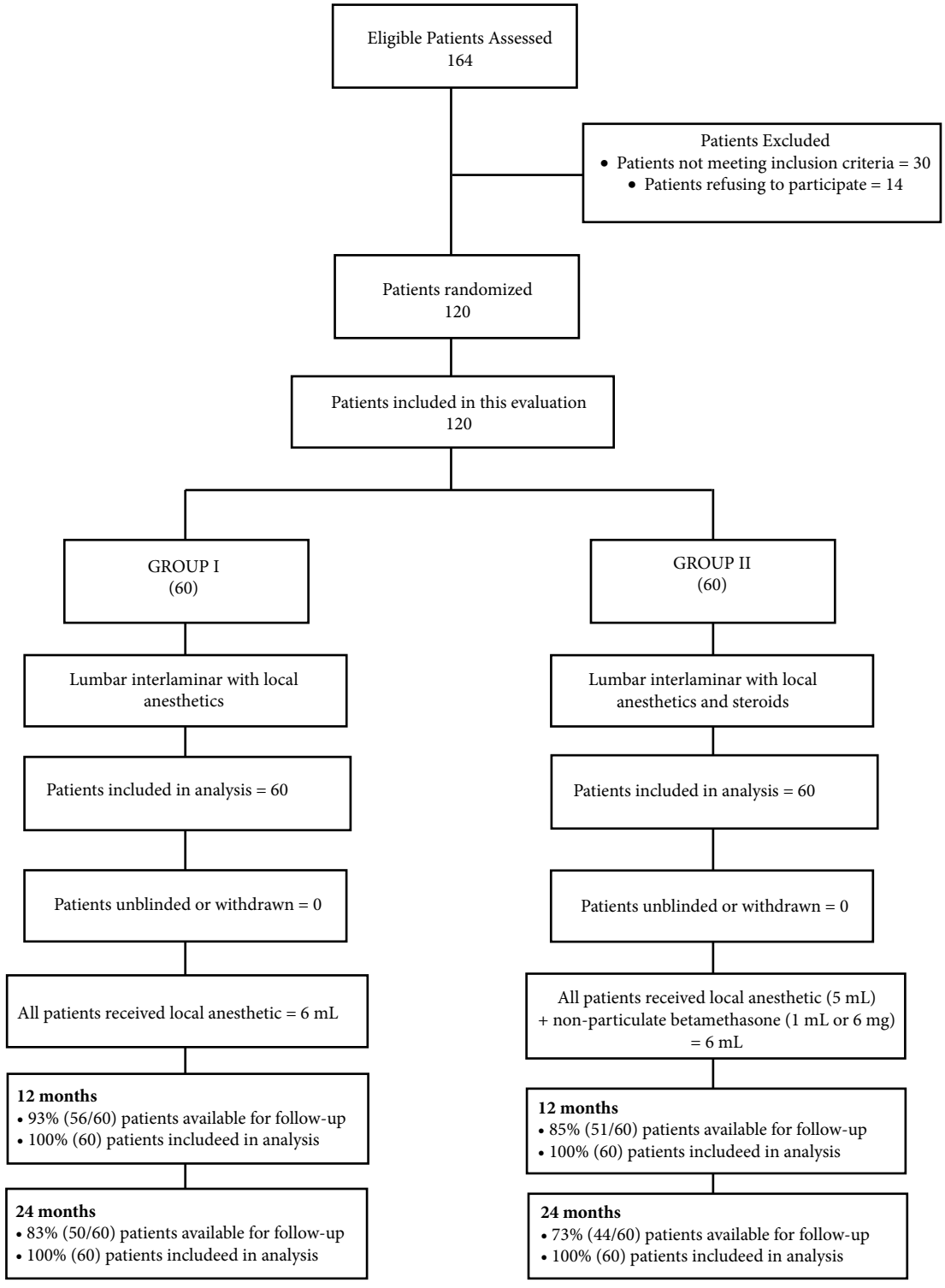

Fig. 1. *Schematic presentation of patient flow at 2-years follow-up.*

Table 1. *Baseline demographic and clinical characteristics.*

		Group 1 (60)	Group II (60)	*P* value
Gender	Male	23% (14)	40% (24)	0.077
	Female	77% (46)	60% (36)	
Age	Mean ± SD	41.2 ± 11.9	42.7 ± 11.4	0.477
Weight	Mean ± SD	211.2 ± 60.9	168.6 ± 40.6	**0.000**
Height	Mean ± SD	65.8 ± 3.7	66.4 ± 4.1	0.430
Duration of Pain (months)	Mean ± SD	104.2 ± 106.5	129.0 ± 90.9	0.173
Onset of Pain	Gradual	67% (40)	70% (42)	0.845
	Injury	33% (20)	30% (18)	
Pain Distribution	Unilateral	20% (12)	25% (15)	0.662
	Bilateral	80% (48)	75% (45)	
Back Pain Distribution	Back pain only	15% (9)	20% (12)	0.849
	Back pain worse than leg pain	65% (39)	60% (36)	
	Leg pain worse than back pain	5% (3)	3% (2)	
	Both equal	15% (9)	17% (10)	
Numeric Rating Score	Mean ± SD	8.0 ± 1.0	7.7 ± .9	0.082
Oswestry Disability Index	Mean ± SD	30.7 ± 4.5	29.2 ± 5.2	0.096

*Multiple patients presented with disc herniation at more than one level.

Table 2. *Comparison of Numeric Pain Rating Scale and Oswestry Disability Index score summaries at 6 time points.*

Time Points	Numeric Pain Rating Scale		Oswestry Disability Index	
	Group I (60)	Group II (60)	Group I (60)	Group II (60)
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
Baseline	8.0 ± 1.0	7.7 ± .9	30.7 ± 4.5	29.2 ± 5.2
3 months	3.6* ± 0.9 (88%)	3.5* ± 1.2 (83%)	14.9* ± 4.3 (83%)	14.6* ± 5.1 (78%)
6 months	3.9* ± 1.1 (77%)	3.6* ± 1.2 (82%)	15.4* ± 4.8 (73%)	14.4* ± 5.2 (77%)
12 months	3.7* ± 1.2 (78%)	3.7* ± 1.3 (72%)	14.9* ± 5.0 (77%)	15.0* ± 6.4 (70%)
18 months	3.8* ± 1.2 (73%)	3.9* ± 1.4 (68%)	14.9* ± 5.0 (75%)	14.9* ± 5.9 (72%)
24 months	3.9* ± 1.3 (73%)	3.6* ± 1.4 (72%)	14.9* ± 5.1 (72%)	14.6* ± 6.1 (70%)
Group Difference	0.378		0.287	
Time Difference	0.000		0.000	
Group by Time Interaction	0.346		0.541	

A lower value indicates a better condition
* significant difference with baseline values within the group (P < 0.001)
(____) illustrates proportion with significant pain relief (≥ 50%) from baseline

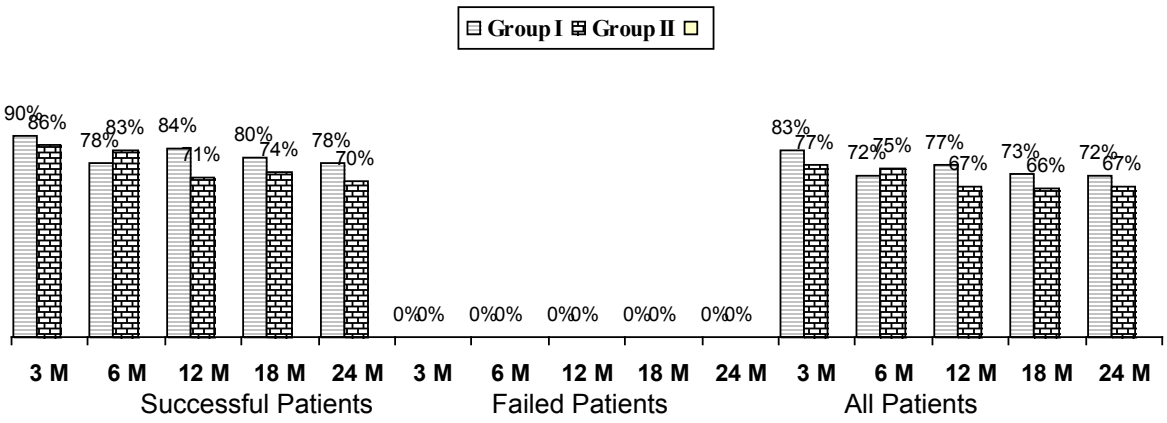

Fig. 2. *Illustration of significant improvement with at least 50% reduction in combined NRS and ODI scores.*

Table 3. *Therapeutic procedural characteristics with procedural frequency, average relief per procedure, and average total relief in weeks over a period of 2 years.*

	Successful Patients		Failed Patients		All Patients	
	Group I (55)	Group II (54)	Group I (5)	Group II (6)	Group I (60)	Group II (60)
Average Number of Procedures for One Year	3.9 ± 0.9	4.0 ± 0.9	1.6 ± 0.9	2.2 ± 1.5	3.7 ± 1.1	3.8 ± 1.1
Average Number of Procedures for 2 Years	6.4 ± 2.2	6.3 ± 2.2	1.6 ± 0.9	2.2 ± 1.5	6.0 ± 2.5	5.9 ± 2.5
For Initial 2 Procedures in Weeks	8.6 ± 10.0	8.2 ± 5.9	0.9 ± 1.0	0.6 ± 0.8	8.2 ± 9.9	7.6 ± 6.0
After Initial 2 Procedures	12.1 ± 3.9	11.9 ± 3.1	2.0	3.5 ± 3.8	12.0 ± 4.0	11.6 ± 3.4
Average Relief Per Procedure	11.5 ± 6.5	11.3 ± 5.1	1.1 ± 1.0	1.5 ± 2.5	11.2 ± 6.6	10.9 ± 5.3
Average Total Relief For One Year (Weeks)	40.0 ± 15.6	39.6 ± 12.4	1.6 ± 1.7	3.2 ± 5.4	36.8 ± 18.4	36.0 ± 16.2
Average Total Relief For 2 Years (Weeks)	73.2 ± 29.3	71.2 ± 29.4	1.6 ± 1.7	3.2 ± 5.4	67.3 ± 34.6	64.4 ± 34.7

Table 4. *Employment characteristics.*

Employment Status	Group I			Group II		
	Baseline	12 Months	24 Months	Baseline	12 Months	24 Months
Employed Part-time	7	5	5	3	5	5
Employed Full-time	5	8	9	11	13	12
Unemployed (Due to pain)	2	1	0	2	0	1
Not Working	3	4	4	3	1	1
Eligible for Employment at Baseline	17	17	17	19	19	19
Total Employed	**12**	**13**	**14**	**14**	**18**	**17**
Housewife	3	3	3	7	7	7
Disabled	39	38	38	32	32	32
Retired/Over 65	1	1	1	2	2	2
Total Number of Patients	**60**	**60**	**60**	**60**	**60**	**60**

Opioid Intake

Table 5 presents the results of repeated measures of analysis for opioid intake. There were significant differences in opioid intake within groups at all times from baseline ($P < 0.01$).

Changes in Weight

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

Adverse Events

Of the 714 lumbar epidural procedures performed, there were 4 subarachnoid punctures that did not result in headache and one patient with nerve root irritation. Also, one patient experienced weight gain due to a high dose of steroid from an unrelated medical problem.

Table 5. *Opioid intake (morphine equivalents in mg).*

Time	Group I (60) Mean ± SD	Group II (60) Mean ± SD
Baseline	57.2 ± 61.4	53.4 ± 53.8
3 Months	35.5# ± 24.2	40.3# ± 35.7
6 Months	36.1# ± 27.0	41.8# ± 37.3
12 Months	36.3# ± 27.0	41.8# ± 37.3
18 Months	36.1# ± 27.0	41.8# ± 37.3
24 Months	36.3# ± 27.0	41.8# ± 37.3
Group Difference	0.377	
Time Difference	0.001	
Group by Time Interaction	0.527	

# indicates significant difference from their baseline values ($P < 0.01$)

Table 6. *Characteristics of changes in weight.*

Weight (lbs)	Group I (60) Mean ± SD	Group II (60) Mean ± SD	P value
Weight at Beginning	211.2 ± 60.9	168.6 ± 40.6	**0.000**
Weight at One Year	211.4 ± 64.0	166.1 ± 40.5	0.000
Change	0.2 ± 13.3	-2.5 ± 10.8	0.227
Lost Weight	37% (22)	57% (34)	0.078
No Change	23% (14)	13% (8)	
Gained Weight	40% (24)	30% (18)	
Weight at 2 years	210.7 ± 64.3	166.9 ± 41.8	**0.001**
Change	-0.46 ± 19.3	-1.6 ± 15.2	0.714
Lost Weight	48% (29)	47% (28)	0.980
No Change	15% (9)	15% (9)	
Gained Weight	37% (22)	38% (23)	

Discussion

Carefully selected patients with axial or discogenic low back pain without disc herniation, radiculitis, facet joint pain or sacroiliac joint pain may respond with significant pain relief and functional status improvement to lumbar interlaminar epidural injections. This randomized, controlled trial of 120 patients followed for 2 years showed significant pain relief and functional status improvement (defined as a 50% decrease in NRS and 50% improvement in ODI scores) showed a 72% success rate in patients receiving local anesthetic and 67% in those receiving local anesthetic with steroids. After the elimination of patients who did not respond,, the successful participants, defined as at least 3 weeks of improvement with the first 2 procedures, showed improvement at 2 years of 78% in local anesthetic group and 70% in the group with local anesthetic and steroids. The results were not significantly different from the one-year follow-up. The results also showed that for 2 years the average procedures were approximately 6 per patient with a significant decrease in opioid intake.

The results of this trial are similar to the results of the trial for caudal epidural injections in axial or discogenic pain that had similar selection criteria (15). However, the results of this trial may be somewhat superior compared to the caudal epidural injections at the end of 2 years where significant improvement was observed in 54% of the patients with local anesthetic and 60% of the patients receiving local anesthetic receiving steroids. After separating the patients into failed and successful outcome groups, the results were similar with reports of 84% and 73% in the caudal trial and 78% and 70% in the present trial of interlaminar epidurals. In the successful group of patients there was a slight superiority with local anesthetic alone compared to local anesthetic and steroids. Furthermore, there was a smaller number of patients in the failed group in the present trial with a total of 5 patients in Group I and 6 patients in Group II, whereas in caudal injection group there were 23 patients in Group I and 19 patients in Group II.

Even though the selection criteria was the same in both groups, we are unable to explain the differences in the higher failure rate for caudal epidural injections

over lumbar interlaminar injections. Overall, the results are very similar in the successful group. Consequently, this trial suggests that in chronic axial low back pain without facet joint pain, disc herniation, radiculitis, or sacroiliac joint pain, lumbar interlaminar injections may be superior to caudal epidural injections with local anesthetic with or without steroids. Thus, the results illustrate that both pain relief and functional status improvement can be achieved with strict selection criteria. Obviously patients suffering with facet joint pain or sacroiliac joint pain would not improve with epidural injections.

The literature is replete with multiple studies and systematic reviews of epidural injections (8); however, there is a continued paucity of literature concerning the evidence for managing axial or discogenic spinal pain.

The results of this trial exemplify the previously published results of epidural injections in axial or discogenic low back pain (8,15,16,69), utilizing fluoroscopy in a contemporary interventional pain management setting. This study is determined as high quality (8) due to proper design, CONSORT guidance, and, most importantly, since there is an active control design. However, multiple systematic reviews have faced criticism for their methodology and inclusion of inappropriate design and trials, leading to inaccurate conclusions (8,70-76). The most quoted and allegedly well designed studies on which the majority of decisions of systematic reviews are based (77,78) have design flaws with all 3 approaches to enter the epidural space in the lumbar spine for managing disc herniation (77-79). Only 2 studies by Ghahreman et al (80) and Gerdesmeyer et al (81) utilized true placebo designs in assessing the role of epidural interventions. In addition, most respected systematic reviews on which the coverage decisions are made (70-72) also utilized methodology that led to inappropriate conclusions, since they considered local anesthetics as a placebo. The role of true placebo, impure placebo, and fake placebos has been extensively discussed (82-84) illustrating the enormous influence of placebo on the interpretation of clinical effects.

In addition, the role of fluoroscopy also has been discussed widely (8). The results of this study are based on procedures performed in a contemporary interventional pain management setting with fluoroscopy. This trial once again demonstrates that epidural injections do not provide permanent long-term relief as claimed by some; however, properly selected patients and appropriate procedures under fluoroscopy can provide long-term improvement which is rather significant with judicious use. Expectations of a single epidural injection providing permanent relief are similar to expecting insulin to provide 6 months of blood sugar control.

The underlying mechanism of action for epidurally administered local anesthetic and steroids has been described, even though it continues to evolve. Historically, epidural steroids have been hypothesized to function by reducing inflammation, thus limiting the indications to compressive radiculopathy or at least radiculitis secondary to chemical irritation (8,20,85-88). Even so, multiple hypotheses have been advanced to explain the mechanism of action of steroids and local anesthetics (8,20,85-93). The evidence shows that steroids, as well as local anesthetics, have significant effects on the modulation of noxious stimulation by various mechanisms. Further, long-term effects are provided by both local anesthetics and steroids or when in combination, in experimental as well as clinical studies (8,51-54,69,93-96).

In patients suffering with chronic low back pain, when utilizing controlled diagnostic blocks, the prevalence of pain due to IDD has been reported to be 39% (9) and 42% (12); primary discogenic pain has been reported in 26% (11) when no other cause was suspected. Sacroiliac joint pain has been established in 10% to 27% of the population (8). Thus, discogenic pain may be diagnosed without discography by eliminating all other structures responsible for pain in axial low back pain even when there are no abnormalities noted in the disc and there is no disc herniation or neural compression identified.

This study may be criticized for its lack of placebo. However, in recent years, comparative effectiveness research has been considered as pivotal to evidence-based medicine (8,70-76). Even though the current study is limited to a single center, and is an active-controlled trial, it is also double-blind and designed to determine whether fluoroscopically directed epidural injections with or without steroids with the usual volumes injected in practice are helpful or not. Consequently, the results of this trial are practical and applicable for interventional pain management settings, highlighting the importance of patient selection and the mode of management with contemporary interventional pain management with repeat procedures only when the pain returns. Placebo control is a difficult aspect of interventional techniques.

The results of this assessment may have far reaching effects on health care delivery. Studies with proper methodology in practical settings are mandatory, but

cost effectiveness is also crucial. Caudal epidural injections have been shown to be cost effective with approximately $2,200 per year of quality-adjusted life year (97). Based on the results of this trial, lumbar interlaminar epidural injections may provide similar results. Health care interventions, specifically interventions related to the spine including interventional techniques, are increasing at an exploding pace (98-104). Some categories of interventional techniques have increased substantially, including lumbar transforaminal epidural injections by 665% from 2000 to 2011 in the Medicare fee-for-service population (103). However, transforaminal epidural injections are not indicated for axial or discogenic pain. Utilization statistics have shown as a group the highest increases for sacroiliac joint injections at 331% (104), followed by facet joint interventions at 308% (104), and epidural injections 130% (103) per 100,000 fee-for-service Medicare recipients.

The results of this assessment are not applicable to the general population unless the same methodology is utilized for the diagnosis and therapy, since the results of this present study are derived from patients in a private interventional pain management practice, undergoing controlled diagnostic blocks, with appropriate selection criteria. The generalizability of these findings might only be possible with studies utilizing larger populations in multiple settings.

Overall, the evidence in this trial demonstrates the effectiveness of lumbar interlaminar epidural injections in managing axial or discogenic chronic low back pain without evidence of disc herniation, radiculitis, facet joint pain, or sacroiliac joint pain.

Conclusion

The results of this trial shows lumbar interlaminar epidural injections of local anesthetic with or without steroids are effective in patients with chronic axial low back pain of discogenic origin without facet joint pain, disc herniation, radiculitis, and/or sacroiliac joint pain.

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