Randomized Trial

Transforaminal Epidural Injections in Chronic Lumbar Disc Herniation: A Randomized, Double-Blind, Active-Control Trial

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Background: The estimated prevalence of lumbar radiculopathy has been described as 9.8 per 1,000 cases of low back pain. There are various surgical and nonsurgical modalities for treating lumbar disc herniation or radicular pain, including epidural injections. Epidural injection administration routes include transforaminal, interlaminar, and caudal approaches. The transforaminal approach requires the smallest volume to reach the primary site of pathology. Systematic reviews have yielded highly variable results, but a recent systematic review showed no significant difference among the 3 approaches.

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

Setting: An interventional pain management practice, a private specialty referral center in the United States.

Objectives: To assess the effectiveness of transforaminal epidural injections of local anesthetic with or without steroids in managing chronic low back and lower extremity pain in patients with disc herniation and radiculitis.

Methods: One hundred twenty patients were randomly assigned to 2 groups: Group I received 1.5 mL of 1% preservative-free lidocaine, followed by 0.5 mL of sodium chloride solution. Group II received 1% lidocaine, followed by 3 mg, or 0.5 mL of betamethasone. The sodium chloride solution and betamethasone were either clear liquids or were provided in opaque-covered syringes.

Outcomes Assessment: The primary outcome measure was significant improvement (at least 50%) measured by the average Numeric Rating Scale (NRS) and the Oswestry Disability Index 2.0 (ODI). Secondary outcome measures were employment status and opioid intake.

Results: At 2 years there was significant improvement in all participants in 65% who received local anesthetic alone and 57% who received local anesthetic and steroid. When separated into non-responsive and responsive categories based on initial relief of at least 3 weeks with 2 procedures, significant improvement (at least 50% improvement in pain and function) was seen in 80% in the local anesthetic group and 73% in the local anesthetic with steroid group.

Limitations: Presumed limitations of this evaluation include the lack of a placebo group.

Conclusion: Transforaminal epidural injections of local anesthetic with or without steroids might be an effective therapy for patients with disc herniation or radiculitis. The present evidence illustrates the lack of superiority of steroids compared with local anesthetic at 2-year follow-up.

Key words: Chronic low back pain, transforaminal epidural injections, disc herniation, radiculitis, lower extremity pain, local anesthetic, steroids

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Low back pain is increasing at an uncontrollable rate, and is the number one contributor to most years lived with a disability (1-6). The prevalence of lumbar radiculopathy, however, is only 9.8 per 1,000 cases (7). While lumbar radiculopathy secondary to disc herniation resolves spontaneously in 23% to 48% of patients, 5% to 15% of patients undergo surgery, resulting in a strain on the health care system and, subsequently, the economy (3-5,8). Various conservative, nonsurgical modalities for treating lumbar disc herniation or radicular pain exist, including epidural injections (9-14). Data from the Spine Patient Outcomes Research Trial (SPORT) evaluation reported the clinical and cost effectiveness of lumbar disc herniation surgery (15-17). Surgery is associated with failure in approximately 25% of patients in well-selected cases. Due to comorbid factors, not everyone who is symptomatic is a surgical candidate; some disc protrusions and small disc herniations are not amenable to surgical interventions (6,18-20). Thus, epidural injections are one of the most common nonsurgical treatments for lumbar disc herniation (10-14).

Epidural injection administration routes include transforaminal, interlaminar, and caudal approaches. The transforaminal approach requires the smallest volume to reach the primary site of pathology. Systematic reviews (6,21-27), guidelines (6,25), and randomized trials (28-33) have been published assessing the efficacy of the 3 approaches of epidural injections in treating lumbar herniated discs and radiculitis. In a recent systematic review assessing epidural injections, short- and long-term efficacy in treating lumbar disc herniation was demonstrated (26). Systematic reviews have demonstrated no significant superiority for transforaminal epidural injections over caudal or interlaminar approaches.

Multiple authors have been critical of some of the various flaws in the systematic reviews and the assessment of included trials. The flaws include combining trials with variable designs and designating active-controlled trials as placebo-control (23-25,34,35). Despite the continued debate and reports of complications (6,22,36,37), transforaminal epidural injections are escalating much faster than caudal and interlaminar procedures combined (10,11). Overall, epidural injections had an annual increase of 7.5% compared to an annual increase of 13.6% for facet joint interventions and an annual increase of 14.2% for sacroiliac joint injections (10).

The present trial assesses the efficacy of lumbar transforaminal epidural injections of local anesthetic with or without steroids, for managing chronic persistent low back and lower extremity pain secondary to disc herniation or radiculitis.

Methods

This trial was conducted in an interventional pain management setting in the United States, a specialty referral center, based on Consolidated Standards of Reporting Trials (CONSORT) guidance (38,39). The approval of the Institutional Review Board (IRB) was obtained and the trial was registered with the U.S. Clinical Trial Registry (NCT 01052571). The design of the trial was randomized, double-blind, and active-control. The trial was conducted with the internal resources of the practice of the first author.

Patients

The required patients for this trial were recruited from the interventional pain management practice of the first author. All eligible patients were provided with the IRB-approved protocol and signed informed consent.

Interventions

The study had 2 groups of randomly assigned patients. Group I patients were treated with 1.5 mL of preservative-free lidocaine 1%, followed by a 0.5 mL sodium chloride solution. Group II patients were treated with preservative-free lidocaine 1% followed by 3 mg of betamethasone, either particulate or nonparticulate.

Pre-Enrollment Evaluation

Demographic data, medical and surgical histories, and co-existing disorders were recorded. All patients underwent a physical examination by the primary author. Pain rating scores using the Numeric Rating Scale (NRS) and functional assessment using the Oswestry Disability Index (ODI) were independently performed by the nurse assessing the patient prior to the enrollment in the trial. Radiologic findings showing disc herniation either based on magnetic resonance imaging (MRI) or computed tomography (CT) were taken into consideration. Work status and opioid intake over the year prior to enrollment were also assessed.

Inclusion and Exclusion Criteria

Inclusion criteria focused on disc herniation and unilateral radiculitis in patients who were at least 18 years old with chronic low back and lower extremity

pain of at least 6 months with pain intensity limiting function and an NRS score above 5 on a scale of 0 to 10. In addition, all patients must have been capable of understanding the trial protocol, able to provide voluntary written informed consent, and had an unrestricted ability to participate in outcomes assessments, including functional status with the ODI. Only disc herniations at L4-5 and L5-S1 were included. All patients must have undergone structured, physician-ordered physical therapy along with an exercise program and nonsteroidal anti-inflammatory therapy.

Exclusion criteria included a history of previous lumbar surgery; radiculitis secondary to spinal stenosis, either foraminal or central; radiculitis without disc herniation; and patients with bilateral radiculitis. In addition, patients with uncontrolled medical illnesses, unstable psychiatric disorders, extremely high dose opioid users not amenable to reductions, and those with an inability to participate in outcomes assessments were excluded. Pregnant and lactating women and patients with a history of or potential for any type of adverse reactions to steroids or local anesthetics were also excluded.

Description of Interventions

All patients were treated in a sterile operating room in an ambulatory surgery center. The procedures were performed by one physician (LM) using appropriate monitoring. Intravenous sedation was provided as indicated.

All injections were performed in a standardized fashion. Patients in Group I received local anesthetic with saline whereas patients in Group II received local anesthetic and steroid. All procedures were performed under appropriate sterile precautions with the patient placed prone. Transforaminal entry was carried out based on the predominant involvement of the nerve root by entering the foramen at the middle or inferior aspect. A 22-gauge Bella-D Coudé® needle was inserted at either L4 or L5, followed by an injection of 0.5 mL of contrast medium and if necessary, additional contrast medium and then an injection of local anesthetic with saline or steroids. For S1 nerve root injection, the S1 foramen was entered, followed by confirmation of the needle placement with contrast medium and then an injection of local anesthetic and saline or steroids. The target points were located under anteroposterior view, adjusting the fluoroscope for optimal exposure. For each nerve root level, 1.5 mL of 1% preservative-free lidocaine followed by 0.5 mL of either sodium chloride solution or betamethasone was injected.

Additional Interventions

All patients were treated based on the protocol. If an emergency situation arose or unblinding was performed, the treatment was altered and the patient was considered withdrawn. If patients were nonresponsive to the injections and were not unblinded, they continued with conservative medical management without unblinding. They also continued their structured exercise program and drug therapy, as did all other patients.

Co-Interventions

Similar co-interventions were provided for all patients, including a structured exercise program. Those employed continued working or returned to work when possible. All patients continued drug therapy with opioids or nonsteroidal anti-inflammatory drugs, although generally, at a lower level than their initial doses. Medications or dosages were changed based on necessity or discontinued if no longer needed. If an increase in opioid dosage was required, the patient was withdrawn. No additional physical therapy, occupational therapy, or any other interventions were offered beyond the protocol.

Objectives

The objective of this trial was to evaluate the effectiveness of local anesthetic lumbar transforaminal epidural injections with or without steroids for managing chronic low back and lower extremity pain with unilateral radiculitis secondary to disc herniation.

Outcomes

The primary outcome was defined as at least 50% average improvement in pain relief and functional status. This outcome measure is robust and also superior to generally utilized measures of 20% or 30% improvement (40). Opioid intake, employment, and work status were considered as secondary outcome measures.

All patients were assessed for primary and secondary outcomes at predefined intervals of 3, 6, 12, 18, and 24 months. In addition, consistent relief lasting at least 3 weeks with the initial 2 epidural injections was considered as responsive, similar to other trials performed with epidural injections, utilizing robust outcome measures (28,29,41-50).

The average NRS was used to measure pain and the average ODI to measure functional ability. On the NRS scale, 0 is no pain and 10 is the worst pain imaginable (51). On the ODI a patient is considered as crippled

and bed-bound or malingering with a score of 80% to 100%; 60% to 80% is considered crippled; 40% to 60% is considered severe disability; 20% to 40% is considered moderate disability; and 0% to 20% is considered minimal disability (52,53). In addition, the value of the NRS and ODI in assessing low back and lower extremity pain in disc herniations have been described (51-54). Opioid intake was calculated by converting into morphine equivalent dosages (55).

For this assessment, we calculated the baseline opioid intake average of the past year (56). We also assigned each patient to one of 4 categories: employable, housewife with no desire to work outside the home, retired, and disabled. The employable category included those who were unemployed due to pain, employed but on sick leave, laid off, or employed at the time of enrollment and subsequent follow-up periods.

Sample Size

A total of 110 patients with a requirement of 55 in each group, with a consideration of a 0.05, 2-sided significance level, a power of 80%, and an allocation ratio of 1:1. We recruited 120 patients with 60 patients in each group, which allowed for a 10% attrition or noncompliance rate.

Randomization and Sequence Generation

A computer-generated random allocation sequence randomized the patients.

Allocation Concealment

The randomization was performed by one of the 3 study coordinators. One of the study coordinators also prepared the drugs and provided them to the operating room nurse. In addition to the computer-generated random allocation sequence with proper concealment, additional measures were also adopted for blinding or masking at all stages of the trial. All medical personnel involved in the care of these patients as well as the patients were blinded to the treatment and allocation sequence. Injections for both groups were clear and indistinguishable from each other (clear nonparticulate betamethasone was used) until September 2012. Because of reports of meningitis related to steroids from compounding pharmacies, commercial betamethasone was used after September 2012. During this period, after injecting local anesthetic, the physician was provided either sodium chloride solution or betamethasone in opaque syringes.

Statistical Methods

Data analyses were carried out using the Statistical Package for Social Sciences version 22 (IBM Corporation, Armonk, NY). Categorical and continuous data comparison, Chi-squared test (Fisher's exact test where necessary) and t test were performed. Because the outcome measures of the patients were measured at 6 points in time, a repeated measures analysis of variance was performed. Univariate analyses of variance with gender, body mass index (BMI), and baseline ODI score as covariates were performed on the reduction in average pain scores and functional improvements between groups. A *P* value of less than 0.05 was considered as statistically significant.

Intention-to-Treat-Analysis

An intention-to-treat analysis was performed wherever the data was missing or was unavailable. The last follow-up or initial data were used for patients who dropped out of the study or for whom no other data were available.

As an additional measure, changes in the NRS were assessed utilizing the last follow-up score, best case scenario, and worst case scenario. Since, there were no significant differences among the various methods, the last follow-up visit was used.

Results

Patient Flow

Patient flow is illustrated in Fig. 1.

Recruitment

The trial recruitment period lasted from January 2010 through December 2011.

Baseline Demographics

Baseline demographic and clinical characteristics are shown in Table 1. There were differences in enrollment with women outnumbering men in Group I. There were also differences in weight and BMI, which were higher in Group I than Group II.

Therapeutic Procedural Characteristics

All injections were performed at L4, L5, and S1. Patients with significant improvement for at least 3 weeks following the initial 2 procedures were considered as successful (Table 2).

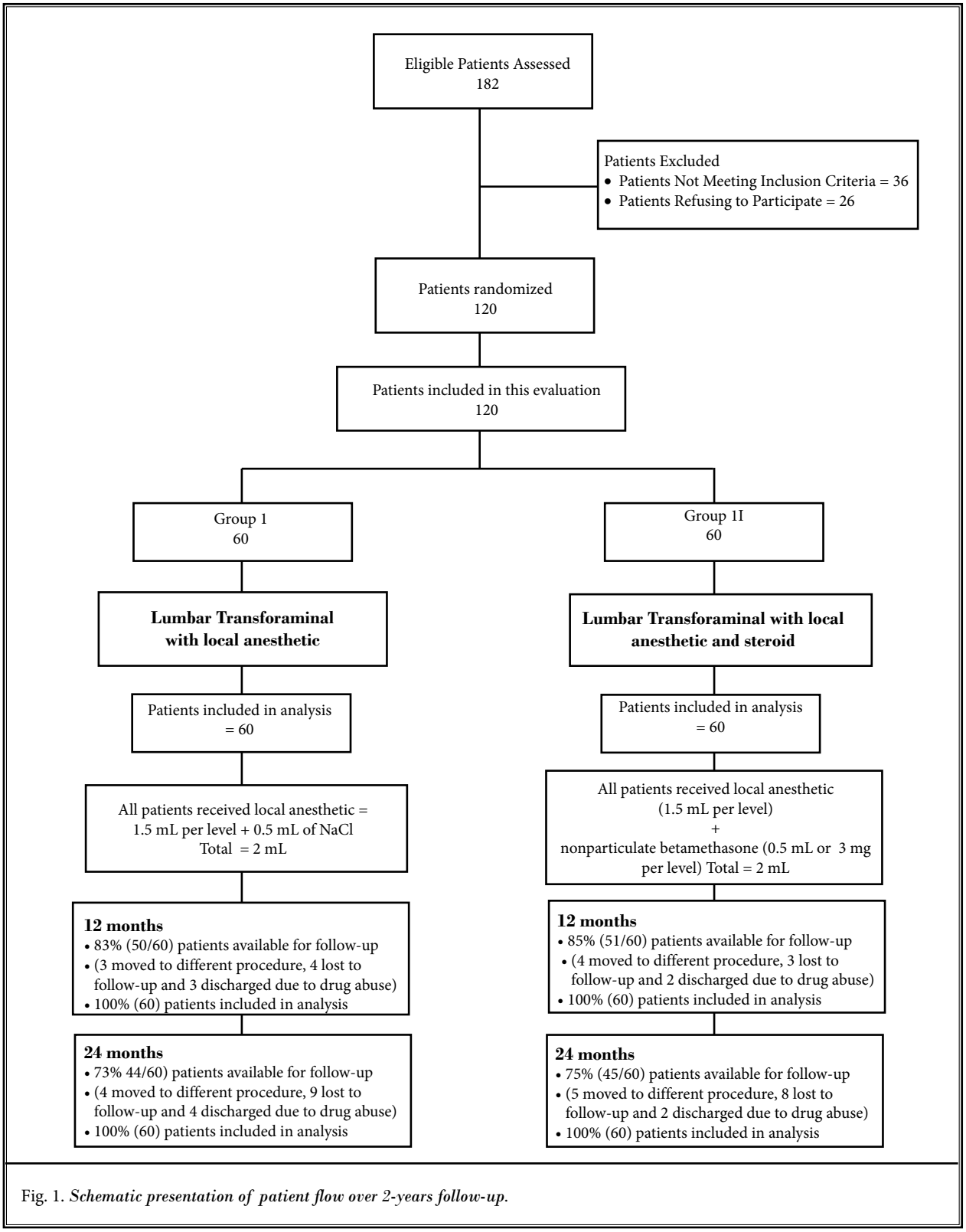

Fig. 1. *Schematic presentation of patient flow over 2-years follow-up.*

Table 1. *Baseline demographic and clinical characteristics.*

		Group 1 (60)	Group II (60)	*P* value
Gender	Men	17% (10)	45% (27)	0.001
	Women	83% (50)	55% (33)	
Age (yrs)	Mean ± SD	43.1 ± 11.8	42.6 ± 11.2	0.794
Weight (lbs)	Mean ± SD	210.1 ± 52.5	167.0 ± 37.7	0.001
Height (inches)	Mean ± SD	65.4 ± 3.6	66.1 ± 3.5	0.272
BMI	Mean ± SD	34.5 ± 7.6	26.8 ± 5.7	0.001
Duration of Pain (months)		98.4 ± 83.4	103.8 ± 92.5	
Mode of Onset of Pain	Gradual	78% (47)	78% (47)	1.000
	Injury	22% (13)	22% (13)	
Disc Herniation * (levels)	L4/5	48% (29)	50% (30)	NA
	L5/S1	72% (43)	65% (39)	
Numeric Rating Score (0-10)	Mean ± SD	8.3 ± 0.9	8.2 ± 0.9	0.529
Oswestry Disability Index (0-50)	Mean ± SD	29.9# ± 4.8	28.0 ± 5.3	0.039

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

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

	Responsive Patients		Non-Responsive Patients		All Patients	
	Group I (49)	Group II (45)	Group I (11)	Group II (15)	Group I (60)	Group II (60)
Average Number of Procedures for One Year	4.0 ± 1.1	3.9 ± 1.1	1.7 ± 0.8	2.1 ± 1.0	3.6 ± 1.4	3.5 ± 1.3
Average Number of Procedures for Two Years	6.0 ± 2.4	5.6 ± 2.5	1.7 ± 0.8	2.4 ± 1.9	5.2 ± 2.7	4.8 ± 2.7
Average Relief for First Procedure in Weeks	4.1 ± 3.2	5.3 ± 9.6	1.1 ± 1.4	1.4 ± 1.8	3.6 ± 3.2	3.9 ± 6.4
Average Relief for Second Procedure in Weeks	8.2 ± 5.0	8.3 ± 4.5	1.3 ± 2.1	1.0 ± 1.0	7.4 ± 5.2	6.7 ± 5.0
Average Relief for Initial 2 Procedures in Weeks	6.1 ± 4.6	6.8 ± 7.7	1.2 ± 1.6	1.2 ± 1.5	5.4 ± 4.7	5.5 ± 7.1
Average Relief per Procedure After Initial 2 Procedures	14.5 ± 7.5	14.1 ± 6.2	1.0 ± 1.4	9.2 ± 5.8	14.3 ± 7.5	13.8 ± 6.2
Average Relief per Procedure (ALL)	11.7 ± 7.7	11.5 ± 7.6	1.1 ±1.6	3.2 ± 4.6	11.1 ± 7.9	10.5 ± 7.8
Average Total Relief for One Year (Weeks)	39.6 ± 12.9	38.5 ± 13.9	2.0 ± 1.9	4.2 ± 6.6	32.7 ± 18.8	29.9 ± 19.4
Average Total Relief for Two Years (Weeks)	69.7 ± 29.0	64.4 ± 33.2	2.0 ± 1.9	7.7 ± 20.0	57.2 ± 37.2	50.2 ± 39.1

Responsive patients – Experienced at least 3 weeks of significant improvement from the first 2 procedures.

Pain Relief and Functional Assessment

Table 3 shows pain relief and functional assessment results.

Figure 2 shows the percentage of patients showing significant improvement with a reduction in NRS and ODI of 50% or more from baseline.

Employment Characteristics

As shown in Table 4, at the end of 2 years, 17 of 17 were employed in Group I (an increase from 29% to 100%), and in Group II, 25 of 26 were employed (an increase from 76% to 96%).

Opioid Intake

Table 5 shows opioid intake decreased from baseline calculated on average intake for one year prior to initiation of treatment to one year and 2 years after.

Changes in Weight

There were significant differences in weight at baseline with Group I patients weighing more than Group II patients. At the end of 2 years, 40% of the patients in Group I and 55% of the patients in Group II lost weight and 40% of the patients in Group I and 28% of the patients in Group II gained weight (Table 6).

Table 3. *Comparison of Numeric Pain Rating Scale and Oswestry Disability Index score for 2 years.*

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	8.3 ± 0.9	8.2 ± 0.9	29.9# ± 4.8	28.0 ± 5.3
3 Months	4.1* ± 1.8 (77%)	4.0* ± 1.5 (73%)	16.5* ± 7.2 (75%)	14.7* ± 6.4 (68%)
6 Months	3.9* ± 1.5 (73%)	4.1* ± 1.7 (68%)	15.2* ± 6.7 (77%)	14.3* ± 6.6 (70%)
12 Months	3.9* ± 1.6 (77%)	4.1* ± 1.6 (63%)	14.7* ± 6.9 (78%)	14.5* ± 6.6 (60%)
18 Months	4.0* ± 1.7 (73%)	4.3* ± 1.6 (58%)	14.9* ± 6.9 (75%)	14.3* ± 6.5 (65%)
24 Months	4.0* ± 1.6 (67%)	4.2* ± 1.6 (58%)	14.9* ± 6.9 (72%)	14.1* ± 6.5 (65%)
Group Difference	0.357		0.278	
Time Difference	0.001		0.001	
Group by Time Interaction	0.613		0.322	

A lower value indicates a better condition.
* significant difference with baseline values within the group ($P < 0.001$).
# significant difference with Group II within the time period ($P < 0.05$).
(_____) illustrates proportion with significant pain relief (≥ 50%) from baseline.

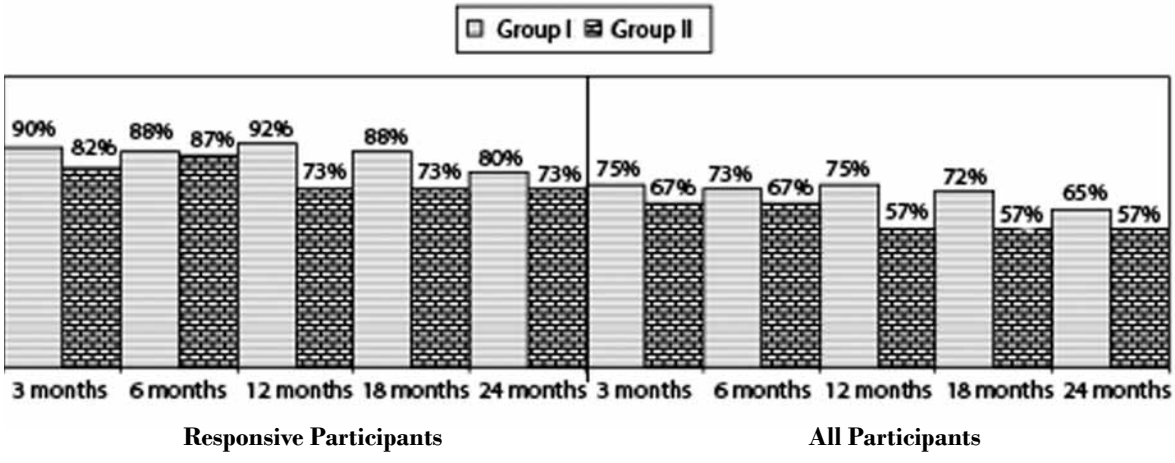

Fig. 2. *Significant reduction (at least 50%) in pain and Oswestry Disability Index from baseline.*

Covariates of Gender, BMI, and Baseline ODI Score

Univariate analyses of variance with gender, BMI, and baseline ODI as a covariate revealed no significant differences in average pain and ODI scores between Groups I and II.

Adverse Events

Of the 601 injections performed, there were 28 (4.6%) intravascular infiltrations and 9 (1.5%) nerve root irritations. There were, however, no post subarachnoid puncture headaches.

Table 4. *Employment characteristics.*

Employment status	Group I			Group II		
	Baseline	12 Months	24 Months	Baseline	12 Months	24 Months
Employed Part-time	2	3	3	9	7	7
Employed Full-time	3	13	14	11	18	18
Unemployed (due to pain)	9	3	3	6	2	2
Unemployed	3	1	1	0	0	0
Eligible for Employment at Baseline	17	17	17	26	26	26
Total Employed	5	16	17	20	25	25
Housewife	10	7	7	0	0	0
Disabled	33	32	31	32	31	31
Retired/Over 65	0	1	1	2	2	2
Total Number of Patients	60	60	60	60	60	60

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

Time	Group I (60) Mean ± SD	Group II (60) Mean ± SD
Baseline	62.9 ± 49.3	68.9 ± 51.9
3 Months	48.6# ± 45.1	40.8# ± 31.8
6 Months	45.3# ± 42.4	39.3# ± 32.2
12 Months	45.1# ± 42.4	38.3# ± 32.2
18 Months	42.6# ± 37.4	36.8# ± 32.3
24 Months	42.93# ± 37.5	36.6# ± 32.4
Group Difference	0.239	
Time Difference	0.001	
Group by Time Interaction	0.496	

Baseline opioid dosage calculated from average intake of last 12 months prior to the first treatment.
# Indicates significant difference from baseline value ($P < 0.05$).

Table 6. *Characteristics of changes in weight.*

Weight (lbs)	Group I (60) Mean ± SD	Group II (60) Mean ± SD	*P* value
Weight at Beginning	210.1 ± 52.5	167.0 ± 37.7	0.001
Weight at One Year	206.9 ± 51.8	164.6 ± 35.8	0.001
Change (reduced)	3.2 ± 14.5	2.4 ± 9.1	0.696
Lost Weight	45% (27)	50% (30)	0.839
No Change	22% (13)	18% (11)	
Gained Weight	33% (20)	32% (19)	
Weight at two years	207.1 ± 54.0	164.9 ± 36.2	0.001
Change (reduced)	3.0 ± 20.3	2.1 ± 10.0	0.754
Lost Weight	40% (24)	55%(33)	0.247
No Change	20% (12)	17% (10)	
Gained Weight	40% (24)	28% (17)	

Discussion

This randomized, active control trial of 120 patients treated with either transforaminal with local anesthetic or transforaminal local anesthetic with steroids with persistent low back and lower extremity pain secondary to disc herniation and radiculitis showed significant improvement in all parameters in both groups. At the end of 2 years, significant improvement was seen in 65% of patients administered local anesthetics alone and 57% of patients administered local anesthetic and steroid when all participants were included. When separated into non-responsive and responsive categories, based on initial relief from 2 procedures lasting at least 3 weeks, significant improvement (at least 50% improvement in pain and function) was seen in 80% in the local anesthetic group and 73% in the local anesthetic with steroid group. Overall relief achieved was 57.2 ± 37.2 weeks over a period of 2 years with 6 procedures when only local anesthetic was administered. Total relief was 50.2 ± 39.1 weeks when local anesthetic and steroid were administered. In the non-responsive groups there were 11 patients in the local anesthetic group and 15 patients in the local anesthetic and steroid group. These results indicate that both treatments are effective but that steroids have no superiority.

The results were superior in the responsive participant group with an average total relief for 2 years of 69.7 ± 29 weeks in Group I and 64.4 ± 33.2 weeks in Group II. Thus, this randomized, active control trial provides evidence that in carefully selected patients, with repeat injections, patients respond to both local anesthetic alone and local anesthetic and steroid.

These results are similar to the published 2-year

results concerning caudal epidural injections and interlaminar epidural injections for lumbar disc herniation management (28,29). However, these results are vastly different from some other published transforaminal epidural trials (30,31,57-61).

The superiority of epidural steroids seen in interlaminar and caudal injections, though mild and short-lived, was not seen in this trial. In this trial, local anesthetic appears to be somewhat better to when compared to local anesthetic and steroid.

This is the only active control trial utilizing lidocaine in chronic disc herniation with radiculitis that repeats the injections based on medical necessity, resulting in an improvement in pain and function of at least 50%.

This trial of transforaminal epidural injections with a 2 year follow-up utilizing a proper methodology in a practical setting provides appropriate information and facilitates the proper application of interventions to improve patients pain and function with a reduction in drug use and potentially a return to the work force. The published cost utility analysis of caudal epidural injections and percutaneous adhesiolysis (33,62) may also be applicable to the results of this trial. It is expected that the cost effectiveness of lumbar transforaminal epidural injections in disc herniation may be 30% to 40% more expensive than caudal epidural injections with estimations based on the setting ranging from $2,600 to $3,000 per one quality adjusted life year (QALY).

In the era of evidence-based medicine and comparative effectiveness research, practical clinical trials with a pragmatic approach are considered to be clinically applicable, valid, and methodologically sound (6,10,24,26,33,63,64). This trial meets the essential criteria for practical clinical trials with an active control group instead of a placebo group, and measures of effectiveness, which is more appropriate than efficacy measured by explanatory trials, improving the applicability of the results in practical interventional pain management settings (65-67). The only efficacy trial performed by Ghahreman et al (31) demonstrates the efficacy of transforaminal epidural injections. The present trial shows clinical and practical results. This trial may be considered the most appropriate available trial in the literature thus far. It may also be criticized for deficiencies, including the lack of a placebo and a larger proportion of patients with a higher BMI in Group I compared to Group II. However, the univariate analysis of variants revealed no significant differences in average pain and ODI scores between Group I and Group II, indicating that these factors had no influence on the outcomes and final interpretation of the results. True placebo design has been difficult to achieve in interventional pain management. This has been achieved only by Ghahreman et al (31) and Gerdesmeyer et al (68). The design by Karppinen et al (57,61) is not an appropriate placebo design. Multiple systematic reviews and guidelines equated local anesthetic with placebo, which is methodologically inappropriate and provides conclusions not based on evidence. There has been extensive discussion on the various interpretations of the role of placebo (69-73). It has been widely described that inactive substances, when injected into active structures, invariably result in various types of clinical effects (74-77). Local anesthetics injected into the epidural space or over the nerves have provided long-term improvement or equal response to steroids in clinical and experimental settings (26-29,41-50,78-87). A systematic review demonstrated similar improvement with local anesthetics or other solutions, including sodium chloride solution, injected into the epidural space (87). It is not only essential to design a proper placebo study, but also mandatory to understand the study design in assessing the evidence. The difficulty with placebo controlled trials is not limited to interventional techniques. Almost all drug trials terminate the placebo groups within 3 months (88).

Disc herniation and radiculitis are based on a pathophysiologic explanation of inflammatory pathology (6,21,24-26,89-95). Epidural steroids have been recommended to be effective in disc herniation and radiculitis secondary to their antiinflammatory profiles. Emerging evidence shows that local anesthetics with or without steroids are equally effective in many settings (21-23,27-29,41-49,78-89).

In summary, the results of this randomized double-blind, active control trial have significant implications for contemporary interventional pain management settings with comparative effectiveness research and cost utility analysis.

Conclusion

The 2-year follow-up results of this randomized, double-blind, active control trial of transforaminal epidural injections of 120 patients with chronic persistent pain from disc herniation who received treatments with local anesthetic alone or local anesthetic and steroid are positive. This trial illustrates the efficacy of these treatments with significant improvement in 65% of patients administered local anesthetic only and 57% of patients administered local anesthetic and

steroid. Efficacy went to 80% and 73%, respectively, in the responsive groups.

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