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Randomized Controlled Trial

Results of 2-Year Follow-Up of a Randomized, Double-Blind, Controlled Trial of Fluoroscopic Caudal Epidural Injections In Central Spinal Stenosis

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Background: Lumbar spinal stenosis is one of the most common causes of low back pain among older adults and can cause significant disability. Despite its prevalence, there is a paucity of literature concerning the treatment of spinal stenosis symptoms. Multiple interventions, including surgery and interventional techniques such as epidural injections and adhesiolysis, are commonly utilized in managing pain related to central spinal stenosis. However, there is a paucity of literature from randomized, controlled trials about the effectiveness of epidural injections for lumbar central spinal stenosis.

Objective: This study sought to assess the effectiveness of caudal epidural injections with or without steroids in providing effective and long-lasting pain relief for the management of chronic low back pain related to lumbar central stenosis.

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

Methods: One hundred patients were randomly assigned to one of 2 groups, with Group I patients receiving caudal epidural injections of local anesthetic (lidocaine 0.5%), whereas Group II patients received caudal epidural injections with 0.5% lidocaine 9 mL mixed with 1 mL of steroid, 6 mg (non-particulate betamethasone).

Outcomes Assessment: Multiple outcome measures, including the Numeric Pain Rating Scale (NRS), the Oswestry Disability Index 2.0 (ODI), employment status, and opioid intake were utilized. Assessments were carried out at 3, 6, 12, 18, and 24 months posttreatment.

The primary outcome was defined as pain relief and improvement in disability scores of 50% or more. Successful treatment was considered as at least 3 weeks of relief following the first 2 injections, categorizing these patients into a successful group, and others into a failed group.

Results: Significant pain relief and functional status improvement were seen in 51% in Group I and 57% in Group II at the end of 2 years in the successful group when the participants were separated into successful and failed groups. However, overall, significant pain relief and functional status improvement (≥ 50%) was demonstrated in 38% in Group I and 44% in Group II at the end of 2 years. The overall number of procedures for 2 years were 4 in both groups, with 5 procedures on average in the successful groups, and approximately 60 weeks of relief in Group I and 54 weeks of relief in Group II at 2 years in the successful group.

Conclusion: Caudal epidural injections of local anesthetic with or without steroids provide relief in a modest proportion of patients undergoing the treatment and may be considered as an effective treatment for a select group of patients who have chronic function-limiting low back and lower extremity pain secondary to central spinal stenosis.

Key Words: Low back pain, lower extremity pain, spinal stenosis, epidural injections, steroids, local anesthetics

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Central lumbar spinal stenosis is defined as a narrowing of the spinal canal with encroachment on the neural structures by surrounding bone and soft tissue, usually caused by spinal degenerative conditions, resulting in significant disability (1-4). However, the causes of spinal stenosis are often multifactorial and the clinical presentation can be variable, and have a lack of correlation with radiographic findings (5,6). The symptoms of lumbar central stenosis range from low back or buttock pain or discomfort to pain and weakness in lower extremities precipitated by walking and prolonged standing (7). Spinal stenosis has been shown to be prevalent in 27.2% of the population in the Framingham study (2). Spinal stenosis is one of the 3 most common diagnoses of low back and leg pain for which surgery is performed, along with intervertebral disc herniation and degenerative spondylolisthesis (8-13). However, lumbar spinal stenosis has been described as the most frequent indication for spine surgery in patients older than 65 years of age (8,11-13). Numerous modalities of treatments have been advocated in managing lumbar central spinal stenosis, including not only surgery with or without fusion, but also interventional techniques and conservative modalities (3,4,11,14-37). Lumbar spinal stenosis is often associated with poor patient health outcomes and functioning, high resource utilization, and substantial health system expenses (4).

The rate of fusion for spinal stenosis has been exploding. Between 2002 and 2007, the frequency of complex fusion procedures for spinal stenosis increased 15-fold from 1.3 to 19.9 per 100,000 Medicare beneficiaries (11). In addition, randomized trials indicate that for severely affected patients, surgery offers greater efficacy than nonsurgical treatments (3,14,15). It has also been shown that multilevel lumbar spinal stenosis without associated degenerative spondylolisthesis or scoliosis can be managed nonoperatively irrespective of the number of levels involved (37). However, in this report, the authors also concluded that if surgery is performed, the number of levels treated does not predict outcome. Thus, even though the results of surgery may be encouraging in severe symptomatic stenosis, the results for patients with mild and moderate stenosis are not well known. They may not only not be candidates for decompressive surgery or fusion, but they may not respond well, and the effects of surgery tend to deteriorate. Next to surgery, epidural injections are one of the most commonly performed interventions for managing chronic low back pain secondary to central spinal stenosis (16,23-35). However, in reference to central spinal stenosis, only one randomized trial has been published thus far with appropriate outcome parameters and fluoroscopic guidance of the epidural injections (16).

This study showed significant improvement in 60% of the patients in the successful group at one year follow-up, whereas overall, the results were 44% of patients receiving local anesthetic only and 46% of patients receiving local anesthetic and steroids, and 60% of patients receiving either local anesthetic alone or with steroids. A randomized, double-blind trial of percutaneous adhesiolysis after failed epidural injections has shown significant pain relief in 76% of the patients at one-year follow-up in the adhesiolysis group compared to 4% of the patients in the control group (35).

In designing a study protocol for lumbar epidural steroid injections for spinal stenosis, Friedly et al (4) described that there was only one early randomized controlled trial (38) which showed no advantage for epidural steroid injections over saline or local anesthetic injections. They also considered the study by Manchikanti et al (39); however, this was a preliminary report of the study, and they misinterpreted the results. They also failed to consider the one-year follow-up which was available at the time of publication (16). For the preliminary report, they described that the study suffered significant methodological limitations, including a lack of statistical power, no primary outcome measure, unblinding of patients and researchers, and a high dropout rate (21/60 patients). However, their assessment was disappointing in that they utilized the number of patients who had not finished their one-year follow-up as dropouts. Further, this (39) was a preliminary publication. Consequently, there was no statistical power. However, primary outcome measures were clearly described and there was no unblinding of patients and researchers. This essentially illustrates the state of evidence-based medicine and comparative effectiveness research with inappropriate methodology and assessment and failure to correct such erroneous assumptions (27,40-46).

However, interventional techniques may be medically indicated and cost-effective as an initial therapy, when there is appropriate selection of the patients and contemporary administration of the intervention. Kuntz et al (47), in an analysis of 10-year cost and health outcomes for persons with stenosis, showed reasonable value for noninstrumented fusion related to laminec-

tomy alone, but unfavorable value for instrumented fusion. The analysis of cost effectiveness after 2 years of the Spine Patient Outcomes Research Trials study (commonly known as SPORT) (15) also showed that stenosis surgeries improved health to a greater extent than nonoperative care, at a cost of $77,600 for a quality-of-life year gained.

Epidural steroid injections are administered by 3 approaches. They are caudal, interlaminar, and transforaminal (32-34). While the majority of the negative evidence for epidural injections has been derived from old studies performed without fluoroscopy, or poorly designed studies, recent evaluations (32-34) have shown significantly different evidence, especially considering those epidural injections performed in contemporary interventional pain management practices with fluoroscopy. Even then, the trials comparing surgical with nonsurgical treatments, specifically epidural injections and trials comparing epidural injections with conservative management, have generally been small and also involved multiple confounding factors with patients suffering not only with spinal stenosis, but also degenerative spondylolisthesis (8,15,48-51).

This study was undertaken to evaluate the role of caudal epidural injections with or without steroids on the significant pain relief and functional status improvement of patients with chronic intractable pain secondary to spinal stenosis. This 2-year follow-up report is an extension of a preliminary report of one-year results previously published (16).

Methods

The study was conducted in an interventional pain management practice, a specialty referral center, in a private practice setting in the United States, and was based on Consolidated Standards of Reporting Trials (commonly known as CONSORT) guidelines (52). The study protocol was approved by the Institutional Review Board (IRB) and was registered with the U.S. Clinical Trial Registry with an assigned number of NCT00370799. This study was conducted with the internal resources of the practice without any external funding, either from industry or from elsewhere.

Patients

One hundred patients were recruited from a single pain management program and were assigned to one of 2 groups. They were given the IRB-approved protocol and informed consent which described in detail all aspects of the study and withdrawal process.

Interventions

Of the 100 patients, 50 patients were assigned to Group I, who received caudal epidural injections of local anesthetic (lidocaine 0.5% preservative-free). Group II (50 patients) received caudal epidural injections of 0.5% lidocaine, 9 mL, mixed with 1 mL of nonparticulate betamethasone, 6 mg. A total volume of 10 mL was injected in each patient, followed by an injection of 2 mL of 0.9% sodium chloride solution to flush the contents from the sacral canal.

Pre-enrollment Evaluation

Demographic data, medical and surgical history with co-existing disease(s), radiologic investigations, physical examination, pain rating scores using the Numeric Rating Scale (NRS), work status, opioid intake, and functional status assessment using the Oswestry Disability Index 2.0 (ODI) were assessed prior to enrollment.

Inclusion and Exclusion Criteria

Only those patients with central spinal stenosis with radicular pain of at least 6 months duration were included. Other criteria were that pain must have been function-limiting, 30 years or older, and the ability to understand the study protocol and provide voluntary, written informed consent and participate in outcome measurement. Another inclusion criterion included failed conservative management.

However, patients with a history of uncontrollable or unstable opioid use, uncontrolled psychiatric disorders, uncontrolled medical illness, those suffering with conditions that could interfere with the interpretation of outcome assessments, pregnant or lactating women, and those with a history or potential for adverse reactions to lidocaine or betamethasone were excluded.

Description of Interventions

One physician performed all epidural injections under fluoroscopy in an ambulatory surgery center, in a sterile operating room. The patients were in the prone position with appropriate monitoring with intravenous access and sedation with midazolam and fentanyl as indicated. Access to the epidural space was obtained utilizing a sterile technique, confirmed by injection of non-ionic contrast medium. After confirmation of the epidural space, an injection of local anesthetic, with or without betamethasone, was administered, followed by an injection of 2 mL of 0.9% sodium chloride solution.

Additional Interventions

Treatments were given to patients as assigned. Upon request, or if an emergency situation arose, a patient would be unblinded. Based on a patient's response to prior caudal epidural injections, and improvement in physical and functional status, repeat caudal epidural injections were administered when increased levels of pain were reported with deteriorating relief below 50%. Unresponsive patients were treated with conservative management and were followed without further epidural injections with medical management, without unblinding.

Co-Interventions

Conservative management utilized by the majority of the patients prior to the interventions included opioid, nonopioid, and adjuvant analgesics and/or a therapeutic exercise program. All these were continued. However, medication adjustments were made based on the medical necessity and indications. Therapeutic exercises and continuation of employment were stressed.

Objectives

The study was designed to assess the effectiveness of caudal epidural injections with or without steroids in managing chronic low back pain with radiculitis secondary to spinal stenosis with long-term follow-up.

Outcomes

Multiple outcome measures were utilized which included the NRS (0–10 scale) pain scale, the ODI on a 0–50 scale, employment status, and opioid intake in terms of morphine equivalents, with assessment at 3, 6, 12,18, and 24 months posttreatment.

The value and validity of the NRS and ODI have been reported (40,53,54). Due to the criticism of outcome measurements and their insignificance (53-55), a robust measure of improvement with significant pain relief and reduction in disability of 50% or more have been utilized in multiple studies and adapted to this study (56-74). Opioid intake was converted into a morphine equivalence (75).

The primary outcome was defined as a significant improvement of 50% or more reduction in the NRS or ODI scores.

Patients responding with relief lasting at least 3 weeks with any of the first 2 procedures were considered to be in the successful category. All others were considered as failures.

The criterion for work status was based on the status at the time of enrollment. Employment categories included: employable, housewife with no desire to work outside the home, retired, and over age 65. Those unemployed because of pain, on sick leave, or laid off were considered employable.

Sample Size

The sample size was calculated based on significant pain relief. Considering a 0.05 2-sided significance level, a power of 80%, and an allocation ratio of 1:1, 18 patients in each group were estimated (76). Allowing for a 10% attrition/noncompliance rate, 40 patients were required.

Randomization

Fifty patients were assigned to each group randomly from a total of 100 patients.

Sequence Generation

A computer-generated simple random allocation sequence was utilized.

Allocation Concealment

Patient randomization and drug preparation was done by one of the 3 study coordinators, without knowledge of the patient, physician, or other personnel.

Implementation

All patients meeting the inclusion criteria were invited to participate. They were enrolled and assigned to a group by a nurse coordinator.

Blinding (Masking)

Group assignments were blinded to all investigators. Study patients were mixed with routine treatment patients.

Statistical Methods

For testing the differences in proportions, chi-squared statistic was used. Wherever the expected value was less than 5, Fisher's exact test was used; a paired t-test was used to compare the pre- and post treatment results of average pain scores and ODI measurements at baseline versus 3, 6, 12, 18, and 24 months. T-test was performed to compare mean scores between groups. A P value of 0.05 was considered as significant. Because the outcome measures of the participants were measured at 6 points in time, repeated measures analysis of variance were performed with the post hoc analysis.

Intent-to-Treat-Analysis

An intent-to-treat-analysis was performed. Either the last follow-up data or initial data were utilized in the patients who dropped out of the study or no other data were available. A sensitivity analysis with changes in the NRS was performed utilizing the last follow-up score, best case scenario, and worst case scenario. If there were no significant differences; the intention-to-treat analysis with last follow-up visit was used.

Results

Participant Flow

Figure 1 illustrates the participant flow.

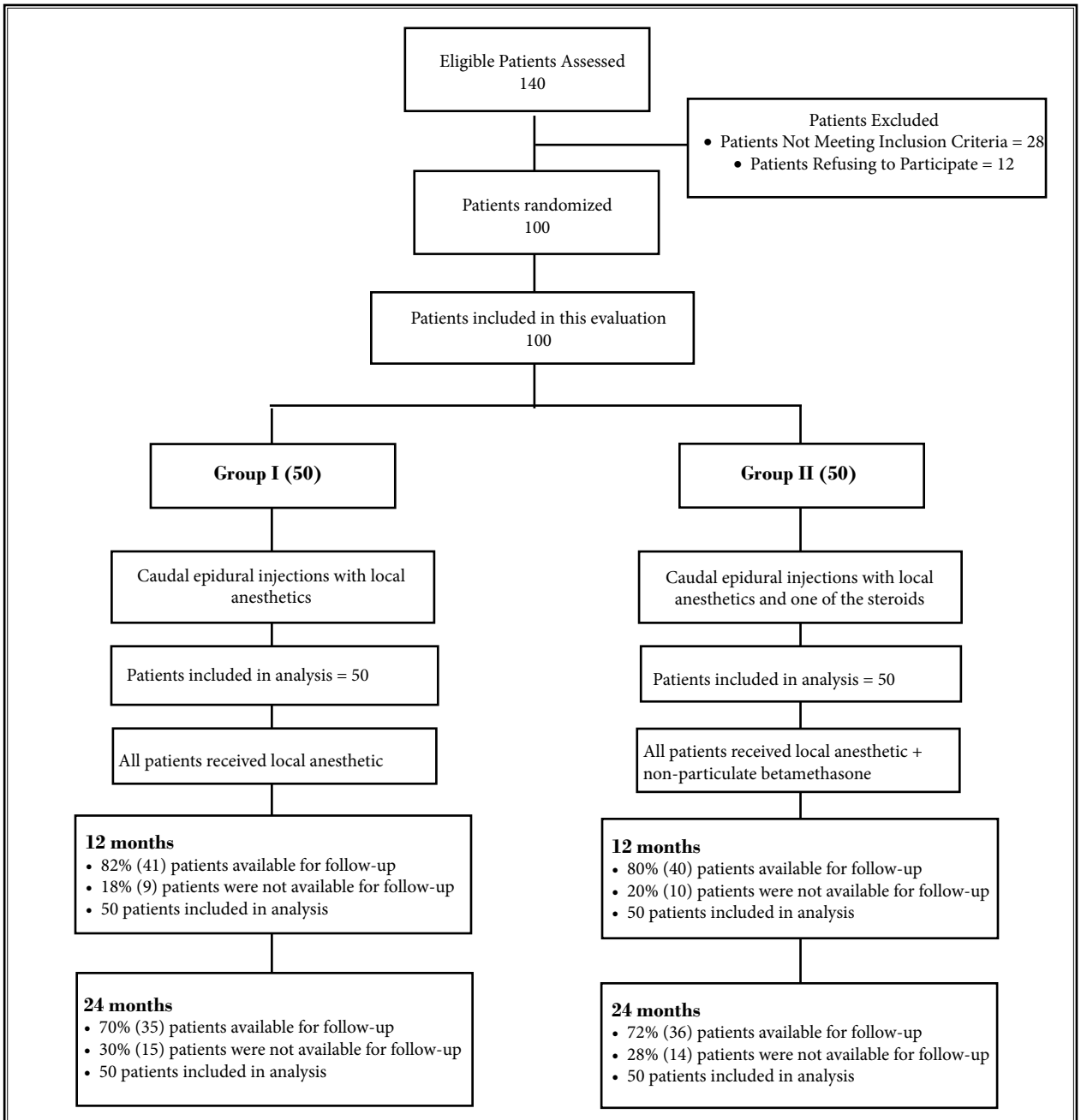

Fig. 1. *Schematic presentation of patient flow at 2-year follow-up.*

Table 1. *Baseline demographic and clinical characteristics.*

		Group 1 (50)	Group II (50)	*P* value
Gender	Male	32% (16)	50% (25)	0.103
	Female	68% (34)	50% (25)	
Age	Mean ± SD	56.9 ± 14.5	55.7 ± 15.9	0.714
Weight	Mean ± SD	195 ± 52.4	187 ± 47.3	0.419
Height	Mean ± SD	66.0 ± 3.7	67.4 ± 3.8	0.069
Duration of Pain (months)	Mean ± SD	94.2 ± 106.9	104.9 ± 80.4	0.479
Onset of the Pain	Gradual	76% (38)	74% (37)	1.000
	Injury	24% (12)	26% (13)	
Pain Distribution	Bilateral	80% (40)	70% (35)	0.356
	Left or Right	20% (10)	30% (15)	
Numeric Rating Score	Mean ± SD	7.9 ± 0.9	7.6 ± 0.8	0.073
Oswestry Disability Index	Mean ± SD	39.8 ± 4.2	28.1 ± 4.6	0.062

Table 2. *Spinal stenosis: Severity and involved level(s) as classified by radiologist(s) (MRI or CT scan).*

	Group	Severe				Moderate				Mild			
		L2/3	L3/4	L4/5	L5/S1	L2/3	L3/4	L4/5	L5/S1	L2/3	L3/4	L4/5	L5/S1
Primary*	I	1	3	5	3	1	8	15	8	3	8	15	7
	II	0	3	10	4	1	5	15	4	2	2	12	6
	Total	1	6	15	7	2	13	30	12	5	10	27	13
Secondary	I	0	0	0	0	0	2	1	0	2	5	5	2
	II	0	0	0	0	1	6	4	0	0	4	2	3
	Total	0	0	0	0	1	8	5	0	2	9	7	5

*Primary - Indicates worst level of stenosis or same type stenosis at multiple levels in patients with multiple level stenosis and all patients with single level stenosis.

Table 3. Number of stenosis levels involved in the study population.

	Group 1	Group II	Total
One Level	19	20	39
Two Levels	20	25	45
Three Levels	9	4	13
Four Levels	2	1	3

Recruitment

Enrollment period lasted from January 2007 to December 2009.

Baseline Data

Table 1 shows baseline characteristics. Tables 2 and 3 illustrate severity and levels of spinal stenosis.

Therapeutic Procedural Characteristics

As shown in Table 4, at 2-year follow-up, Group I had an average overall pain relief of 44.6 ± 42.3 weeks; whereas Group II patients reported 41.5 ± 40.5 weeks of relief. However, when participant were separated into successful and failed categories, the relief was 59.6 ± 40.41 weeks in Group I and 54.2 ± 38.3 weeks in Group II in the successful categories at 2-year follow-up. The average number of procedures was 5.1 ± 2.6 per 2 years in Group I and 4.5 ± 2.3 in Group II in the successful categories. In contrast, in the failed category, the number of procedures per 2 years was 1.7 ± 0.6 in Group I and 1.6 ± 1.4 in Group II.

Outcomes

Pain Relief and Functional Improvement

Table 5 and Figure 2 illustrate the proportion of participants with a significant change in pain and func-

Table 4. *Therapeutic procedural characteristics with procedural frequency, average relief per procedure, and average total relief in weeks over a period of 2 years.*

	Successful subjects		Failed subjects		Combined	
	Group I (37)	Group II (37)	Group I (13)	Group II (13)	Group I (50)	Group II (50)
Procedural details						
Average number of procedure per one year	3.6 ± 1.1	3.5 ± 1.2	1.7 ± 0.6	1.4 ± 0.7	3.1 ± 1.3	2.9 ± 1.4
Total Number of injection in one year	133	128	22	18	155	146
Average number of procedure per two years	5.1 ± 2.6	4.5 ± 2.3	1.7 ± 0.6	1.6 ± 1.4	4.2 ± 2.7	3.8 ± 2.4
Total Number of injection in two years	189	168	22	21	211	189
Relief details						
Average relief per procedure for initial 2 procedures in weeks	10.1 ± 15.4	8.11 ± 12.4	1.2 ± 2.0	1.0 ± 1.8	8.1 ± 14.0	6.8 ± 11.6
Average relief per procedure after initial 2 procedures	12.7 ± 6.7	15.0 ± 10.9	0.0	12.8 ± 1. 3	12.6 ± 6.8	14.9 ± 10.7
Average relief per injection	11.7 ± 10.9	11.9 ± 12.1	1.1 ± 2.0	3.2 ± 5.0	10.6 ± 10.9	11.0 ± 11.8
Average total relief per one year (weeks)	34.0 ± 16.3	31.7 ± 17.5	1.9 ± 2.4	2.1 ± 4.7	25.6 ± 19.9	24.0 ± 20.0
Average total relief per two years (weeks)	59.6 ± 40.1	54.2 ± 38.8	1.9 ± 2.4	5.2 ± 15.6	44.6 ± 42.3	41.5 ± 40.5

# indicates significant difference group II ($p < 0.05$)
Successful subject : At least 3 weeks of relief following the first 2 injections

Table 5. *Comparison of Numeric Pain Rating Scale for pain and Oswestry Disability Index score summaries at six time points (lower value indicates better condition).*

Numeric Rating Score	Numeric Pain Rating scale		Oswestry Disability Index	
	Group I (50) Mean ± SD	Group II (50) Mean ± SD	Group I (50) Mean ± SD	Group II (50) Mean ± SD
Baseline	7.9 ± 0.9	7.6 ± 0.8	29.8 ± 4.2	28.1 ± 4.6
3 months	4.1* ± 1.8 (66%)	4.1* ± 1.9 (62%)	17.2* ± 6.8 (58%)	16.8* ± 7.9 (49%)
6 months	4.1* ± 1.7 (58%)	4.2* ± 1.9 (56%)	17.2* ± 7.3 (54%)	16.9* ± 8.2 (50%)
12 months	4.4* ± 1.8 (48%)	4.3* ± 2.0 (46%)	17.5* ± 7.6 (50%)	16.9* ± 7.8 (50%)
18 months	4.5* ± 1.8 (44%)	4.4* ± 2.0 (48%)	17.6* ± 7.2 (42%)	16.7* ± 7.9 (48%)
24 months	4.6* ± 1.8 (42%)	4.7* ± 2.2 (44%)	17.5* ± 7.3 (42%)	17.0* ± 7.6 (46%)
Group Difference	0.795		0.598	
Baseline vs follow-up points	0.000		0.000	
Group by Time Interaction#	0.726		0.572	

Percentages in parenthesis illustrates proportion with significant pain relief (≥ 50%) from baseline
* indicates significant difference with baseline values ($P < 0.05$)
# Group by Time Interaction - There were no significant difference between groups at 3 months, 6 months, 12 months, 18 months and 24 months.

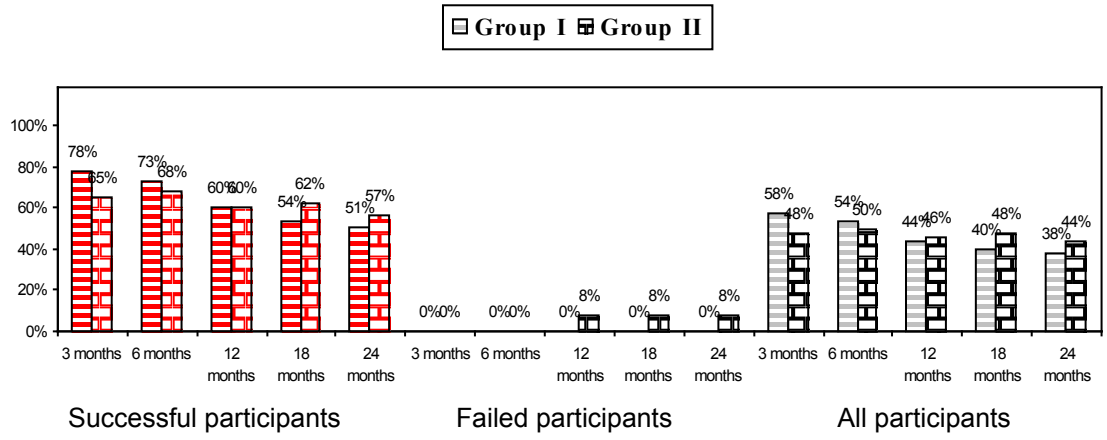

Fig. 2. *Proportion of patients with significant reduction in Numeric Rating Score and Oswestry Disability Index (>= 50% reduction from baseline).*

Table 6. *Employment characteristics.*

Employment status	Group I (50)			Group II (50)		
	Baseline	12 months	24 months	Baseline	12 months	24 months
Employed part-time	1	2	1	1	1	1
Employed full-time	4	3	4	7	9	9
Unemployed	1	0	0	2	1	1
Unemployed due to pain	1	1	1	1	0	0
Total Employed	**5**	**5**	**5**	**8**	**10**	**10**
Eligible for employment	7	7	7	11	11	11
Housewife	2	2	2	4	4	4
Disabled	30	30	30	18	18	18
Over 65 year of age	11	12	12	17	17	17
Total Number of Patients	**50**	**50**	**50**	**50**	**50**	**50**

tion. This is illustrated for all participants with 38% in Group I and 44% in Group II at 24 months. However, the data from the successful categories showed improvement in 51% in Group I and 57% in Group II.

Employment Characteristics

Employment characteristics are shown in Table 6.

Opioid Intake

Results of opioid intake over a period of 2 years are illustrated in Table 7.

Changes in Weight

Changes in weight over a 2-year period in both groups are illustrated in Table 8.

Adverse Events

There were no major adverse events reported over a period of 2 years in 100 patients (400 encounters).

Discussion

The current study of 100 patients with lumbar central spinal stenosis with a 2 year follow-up with per-

Table 7. *Opioid intake (morphine equivalence mg)*

Narcotic intake (Morphine Equivalence mg)	Group I (50)	Group II (50)
	Mean ± SD	Mean ± SD
Baseline	45.66 ± 53.0	49.2 ± 42.2
3 months	33.3* ±35.7	33.1* ± 27.5
6 months	34.4 ± 43.0	33.7* ± 34.7
12 months	35.9 ± 43.1	33.3* ± 34.5
18 months	35.7 ± 43.3	33.3* ± 34.5
24 months	35.7 ± 43.3	32.5* ± 34.8
Group Difference	0.895	
Baseline vs follow-up points	0.012	
Group by Time Interaction#	0.405	

* indicates significant difference with baseline values ($p < 0.05$)
# Group by Time Interaction - There were no significant difference between groups at 3 months, 6 months, 12 months, 18 months and 24 months

Table 8. *Characteristics weight monitoring.*

Weight (lbs)	Group I (50)	Group II (50)	*P* value
	Mean ± SD	Mean ± SD	
Weight at Beginning	195± 52.4	187 ± 47.3	0.419
At one year			
Weight at one year	193 ± 53.8	185 ± 47.4	0.458
Change from baseline	-2.4 ± 9.0	-1.8 ± 8.11	0.728
No change	24% (12)	26% (13)	0.910
Gained weight	34% (17)	30% (15)	
Lost weight	42% (21)	44% (22)	
At 2 years			
Weight at 2 years	192 ± 52.8	187 ± 47.3	0.546
Change from baseline	-2.9 ± 9.1	-0.9 ± 9.2	0.277
No change	32% (16)	26% (13)	0.741
Gained weight	28% (14)	34% (17)	
Lost weight	40% (20)	40% (20)	

sistent, severe, chronic low back and lower extremity pain responded to caudal epidural injections with or without steroids with significant pain relief and functional status improvement in 51% in Group I with local anesthetic only, and 57% with local anesthetic and steroids in Group II at the end of 2 years when patients were categorized into successful group with response of at least 3 weeks with first 2 procedures. Overall significant improvement above 50% was seen in 38% of the patients in Group I without steroids and 44% of the patients in Group II with steroids at 2-year follow-up. The procedures for 2 years in the successful category were 5.1 ± 2.6 in Group I and 4.5 ± 2.3 in Group II with average total relief per two year of 59.6 ± 40.1 weeks in Group I and 54.2 ± 38.8 weeks in Group II over a period of 104 weeks. However, the overall total relief per 2 years was 44.6 ± 42.3 weeks in Group I and 41.5 ± 40.5 weeks in Group II among all participants including the very low response seen in failed participants. Thus, there were no differences between the participants receiving either local anesthetic alone or local anesthetic with steroids. Consequently, the results of this study show that if the response is poor with the first 2 procedures, future treatments will continue to obtain a very poor or no response. Overall, the response is only modest in approximately half of the patients feeling significant improvement half of the time.

The results of this study may not be compared to previous evaluations as there are no other randomized trials available for caudal epidural injections. The results of this study show that with appropriate patient selection and prudent use of repeat injections, long-term relief can be achieved – though modest.

This study is significant for interventional pain management practices, pragmatic, or practical clinical trials, with an active-control measure effectiveness, and so are superior to explanatory trials that measure efficacy (77,78). This is the first large scale study utilizing an active-control design with a follow of 2 years.

The study may face criticism with or without appropriate understanding of the design and the results (4). The study may be criticized for the lack of a placebo group. There are numerous difficulties associated with placebo control which are insurmountable with interventional techniques in the United States. A true placebo, meaning an inactive substance placed in an inactive structure – away from nerves and closed spaces, is not only rare but almost impossible. Further, placebo controlled neural blockade is not realistic and has been widely misinterpreted (25-27,40-46,52-74,79). Multiple authors, specifically methodologists, have mistakenly reported that any local anesthetic injection, which yields similar results as steroids, is considered as placebo (25-27,40-46,53). In contrast, the experimental and clinical evidence shows active response which may yield to inaccuracies, even with sodium chloride solution, along with local anesthetic injection or other substances (80-82). In addition, epidural saline has been

shown to be active and therapeutic (83-85). However, a proper placebo design has been utilized by Ghahreman et al (86). The numerous interactions with placebo and nocebo effects are misunderstood and inappropriately applied by methodologists (87,88). Further, it would be inconceivable for a placebo effect to last for 2 years, on some occasions in 85% of the patients, with repeat interventions. Another argument relates to the natural healing process and confounding of the results. However, this has not been the case in these patients as these patients have suffered over long periods of time and were recalcitrant and non-responsive to other modalities of treatments.

It has been clearly shown in numerous studies that local anesthetics and steroids exert analgesic effects by various mechanisms and there may not be significant difference whether steroids are used or not (89-93). However, multiple other substances also have been evaluated in recent years (94-96). Further, in an evaluation by Golish et al (97) showed that presence of a molecular complex of fibronectin and aggrecan predict response to lumbar epidural steroid injections for radiculopathy with herniated nucleus pulposus. They concluded that this biomarker is accurate, objective, and not affected by demographic or psychosocial variables in the small series they published in lumbar disc herniation with radiculitis. No such evaluations have been performed in patients with spinal stenosis and also there are no large scale studies to replicate the data by Golish et al. Multiple complications with epidural steroid injections have been reported which included complications related to the steroids, placement of the needle, injection of various drugs, bleeding, fasting, and infection. However, none of these were observed in this evaluation (98-102).

In summary, the evidence in this evaluation of a randomized, active-controlled trial demonstrates that caudal epidural injections with or without steroids in patients with spinal stenosis with low back and lower extremity pain provide significant pain relief and improvement in functional status at 2-year follow-up.

Conclusion

This 2-year report of the results of a randomized, double-blind trial of caudal epidural injections with local anesthetic with or without steroids for chronic function-limiting low back pain and lower extremity pain secondary to spinal stenosis has demonstrated pain relief and improvement in functional status in 51% of participants in local anesthetic group and 57% in local anesthetic with steroid group in the successful category.

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