Randomized Trial

Fluoroscopic Epidural Injections in Cervical Spinal Stenosis: Preliminary Results of a Randomized, Double-Blind, Active Control Trial

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Background: Cervical spinal stenosis is a common disease that results in considerable morbidity and disability. There are multiple modalities of treatments, including surgical interventions and multiple interventional techniques including epidural injections. The literature on the effectiveness of cervical epidural steroids is sporadic. Emerging evidence for cervical interlaminar epidurals for various conditions in the cervical spine is positive; however, the effect of fluoroscopic epidural injections in cervical spinal stenosis has not been studied.

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

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

Objectives: To evaluate the effectiveness of cervical interlaminar epidural injections with local anesthetic with or without steroids in the management of chronic neck pain with upper extremity pain in patients with cervical central spinal stenosis.

Methods: Patients with cervical central spinal stenosis were randomly assigned to one of 2 groups: injection of local anesthetic only or local anesthetic mixed with non-particulate betamethasone. Sixty patients were included in this analysis. Randomization was performed by computer-generated random allocation sequence by simple randomization.

Outcomes Assessment: Multiple outcome measures were utilized including the Numeric Rating Scale (NRS), the Neck Disability Index (NDI), employment status, and opioid intake with assessment at 3, 6, and 12 months post-treatment. Significant pain relief or functional status was defined as a 50% or more reduction of NRS or NDI scores.

Results: Significant pain relief was seen in 73% in Group I and 70% in Group II, in Group II showing both significant pain relief and functional status improvements. Group I's average relief per procedures was 11.3 ± 5.8 weeks; for Group II it was 8.6 ± 3.6 weeks, whereas after initial 2 procedures, average relief was 13.7 ± 8.7 weeks in Group I, and 13.6 ± 4.7 weeks in Group II. In the successful group, the average total relief in a one-year period was 42.2 ± 14.7 weeks in Group I and 34.3 ± 13.4 weeks in Group II, with 76% in Group I and 77% in Group II.

Limitations: Study limitations include the lack of a placebo group and that this is a preliminary report of only 60 patients, 30 in each group.

Conclusion: Patients who have chronic function-limiting pain that is secondary to cervical central stenosis might receive relief with cervical interlaminar epidurals of local anesthetic, whether with or without steroids.

Key words: Chronic neck pain, cervical disc herniation, cervical stenosis, cervical central stenosis, cervical epidural injections, epidural steroids, local anesthetics

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Chronic recurrent neck pain in adults is common. The 12-month prevalence is 30% to 50%; intense pain and disability are seen in 14% of adults (1-3). Common causes include cervical spondylosis, cervical disc herniation, cervical stenosis, cervical facet joint arthritis, radiculopathy, and cervical discogenic abnormalities (4-7).

Cervical spinal stenosis is a common disease that results in considerable morbidity and disability (8-10). Degenerative change is the most common cause of cervical stenosis and can be due to disc herniation, osteophyte formation, or a combination of both, namely disc-osteophyte complex (8). Tandem spinal stenosis (TSS) is a degenerative disease that describes a double stenotic lesion involving the cervical and lumbar spine (11,12). Historically, TSS accounts for between 5% and 25% of all cases of stenosis (11,12). However, cervical spinal stenosis is less common than lumbar spinal stenosis. With increasing age, a large proportion of the population exhibit radiological signs of discopathy or spondylosis, leading to constriction of the spinal canal (9). Thus, cervical spinal stenosis has been detected in 26% of asymptomatic group of older individuals (13)

Despite multiple modalities of treatments, including surgical interventions and various other modalities for diagnosis and treatment of spinal pain, with exploding health care costs, the treatment modalities for cervical spinal stenosis have not been well described (1,3-6,11,12,14-40). Apart from surgical interventions, epidural steroid injections are one of the most common interventions in the non-surgical management of neck and upper extremity pain secondary to disc herniation and radiculitis, spinal stenosis, post surgery syndrome, and discogenic pain (1,14-20,25,41-43).

Benyamin et al (1) in a systematic review of cervical interlaminar epidural injections determined that the evidence was moderate in managing chronic neck and upper extremity pain; however, this evidence has been related to mostly disc herniation and radiculitis even though some studies have included patients with different etiologies. Further, Manchikanti et al in 2 studies, in their preliminary reports (14,25) showed the effectiveness of cervical interlaminar epidural injections with or without steroids in over 75% of the patients with axial neck pain or disc herniation and radiculitis. Even then, the evidence has been questioned and continues to be debated similar to lumbar epidural injections due to the design of the studies, fluoroscopic utilization, study size, outcome parameters, duration of follow-up, and bias exerted peer reviews, along with inappropriate methodology, leading to inappropriate conclusions (1,20). A Cochrane review of medicinal and injection therapies for mechanical neck disorders (37) have shown no significant evidence for cervical epidural injections. However, the role of epidural injections in managing chronic persistent pain of cervical spinal stenosis has not been evaluated.

Evaluating the role of cervical interlaminar epidural injections with or without steroids in a certain patient population is the present study's purpose—specifically, in patients who have chronic, function-limiting neck pain and disability secondary to central cervical spinal stenosis. This preliminary report describes data from 60 patients who have completed a one year follow-up; the full report will have data on 120 patients.

Methods

The present study was performed in the United States in a private pain management practice and specialty referral center. Consolidated Standards of Reporting Trials (CONSORT) guidelines were followed (44). The Institutional Review Board (IRB) approved the study's protocol; the study is registered with the U.S. Clinical Trial Registry, NCT01071369.

Participants

New patients presenting for interventional pain management were recruited for the study and assigned to one of two groups.

Interventions

Both groups received cervical interlaminar epidural injections. Group I patients received 5 mL of 0.5% lidocaine; Group II received 4 mL of 0.5% lidocaine mixed with 1 mL or 6 mg of nonparticulate betamethasone.

The IRB-approved protocol and informed consent, which describe the study in detail, were given to the patients.

Pre-enrollment Evaluation

A pre-enrollment evaluation was conducted. Data collected during the evaluation included work status, demographic data, opioid intake, physical examination, medical and surgical history with coexisting disease(s), Numeric Rating Scale (NRS) pain rating scores, functional status assessment with the Neck Disability Index (NDI), and radiologic investigations.

Inclusion and Exclusion Criteria

Inclusion criteria were a diagnosis of cervical central spinal stenosis with or without foraminal stenosis, patients over 30 years old and with a history of chronic function-limiting neck pain and upper extremity pain of at least 6 on a scale of 0-10, pain for at least 6 months in duration, and patients who were competent to understand the study protocol and provide voluntary, written informed consent, and participate in outcome measurements.

Further inclusion criteria included patients who failed to improve substantially with conservative management including, but not limited to, physical therapy, chiropractic manipulation, exercises, drug therapy, and bed rest.

Exclusion criteria were a history of cervical spinal surgery, foraminal stenosis without central stenosis, uncontrollable or unstable opioid use, uncontrolled psychiatric disorders, uncontrolled medical illness (either acute or chronic), any conditions that could interfere with the interpretation of the outcome assessments, pregnant or lactating women, and patients with a history or potential for adverse reaction(s) to local anesthetics or steroids.

Description of Interventions

A single physician performed all procedures in an ambulatory surgery's sterile operating room. Patients were prone, appropriately monitored, and sedated with midazolam and fentanyl. Under fluoroscopy, the epidural space between C7 and T1 to C5 and C6 was entered, using the loss of resistance technique and confirmed with nonionic contrast medium. Then, the appropriate injection, based on the group the patient was assigned, was made.

Additional Interventions

Patients remained blinded unless they requested unblinding or if an emergency arose. Treatments were performed as assigned. Additional cervical epidural injections were given depending on a patient's response. Nonresponsive patients continued conservative management without further injections, unless they requested unblinding.

If physical and functional status improved, then repeat injections were given. Also, only when there was increased pain and deteriorating relief below 50% were repeat injections given.

Co-Interventions

Patients did not receive bracing, specific physical or occupational therapy, or any intervention other than the assigned study intervention. However, patients did continue exercise programs already started as well as their occupation. Most were already taking adjuvant analgesics, both opioid and nonopioid. If they improved enough, these adjuvants were either stopped or dosages decreased. For some, dosages were increased.

Objectives

This study seeks to evaluate whether cervical epidural injections, with or without steroids, are effective for managing pain caused by chronic neck and upper extremity pain secondary to cervical central spinal stenosis.

Outcomes

The following outcomes were measured at baseline and at 3, 6, and 12 months post-treatment: opioid intake measured in morphine equivalent; work status; NDI; and NRS.

Pain relief of 50% associated with a 50% improvement in NDI was considered significant. The NRS and NDI have been shown to be valid and reliable in patients with mechanical neck pain (45-47).

Morphine equivalents were used to measure opioid intake (48).

Patients unemployed due to pain and those employed only part-time due to pain were considered employable. Those not working, but not due to pain, including those retired or who chose not to work and homemakers were not considered employable.

Sample Size

The sample size needed for each group was determined to be 60 patients. This is based on a 10% attrition/noncompliance rate, as well as a 0.05 two-sided significance level, a power of 80%, and a 1:1 allocation ratio (49). Fifty to 60 patients in a group is considered appropriate (50-61).

Randomization

Sixty patients are expected to be randomly assigned to each group.

Sequence Generation

A computer-generated random allocation sequence performed the randomization.

Allocation Concealment

Patient randomizing and appropriate drug preparing were done by an operating room nurse who assisted with the procedure.

Implementation

If they met inclusion criteria, patients were invited to become study participants. A nurse assigned as one of the study's 3 coordinators enrolled them and gave them their group assignment.

Blinding (Masking)

Group assignments were blinded to the participants and the physicians performing the interventions. The injectates were clear; it was impossible to tell if it contained steroid. Also, participants were mixed with patients not enrolled in the study who were presenting for routine treatment. The physician was not informed who was and who was not a study participant. A statistician not involved with patient care selected those chosen for one-year follow-up. If unblinding did occur, the physician and other patients were not informed, thus preserving the integrity of the blinding.

Statistical Methods

Four statistical analyses were performed: for differences in proportions, Chi-squared statistic; if the expected value was less than 5, Fisher's exact test; t test for comparing mean scores between groups; paired t test for comparing pre- and post-treatment average pain scores and NDI measurements at baseline against scores at 3, 6, and 12 months. Statistical significance was $P < 0.05$.

Intent-to-Treat-Analysis

The last follow-up data or initial patient data from study dropouts was used for the intent-to-treat analysis. A sensitivity analysis used best and worst case scenarios and last follow-up scores.

Results

Participant Flow

Figure 1 illustrates the participant flow.

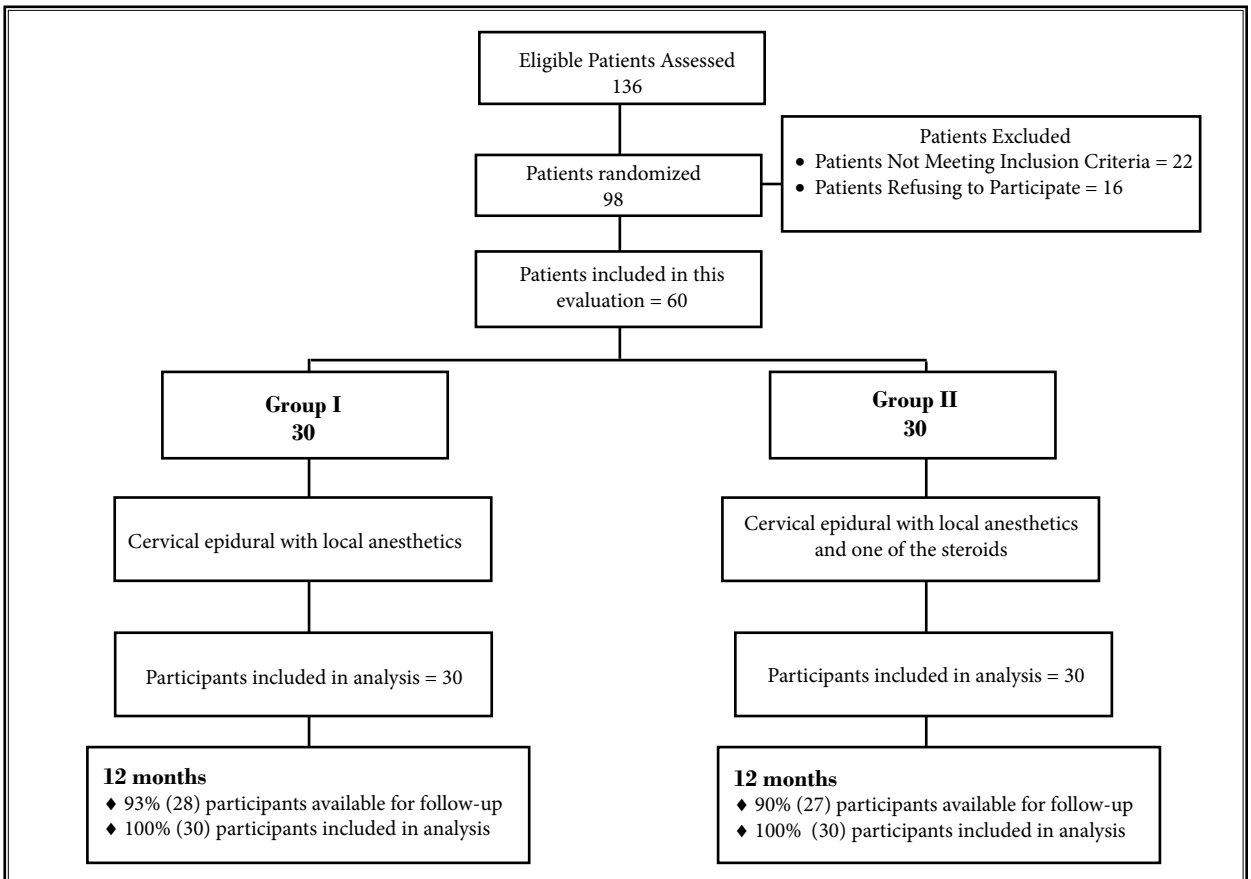

Fig. 1. *Schematic presentation of patient flow.*

Recruitment

Enrollment period started in August 2007 and continues.

Baseline Data

Table 1 shows baseline characteristics. There were no significant differences observed in any of the aspects except mean weight which was higher in Group I compared to Group II.

Tables 2 and 3 illustrate severity and levels of spinal stenosis.

Analysis of Data

Intention-to-treat analysis was carried out by last follow-up data, as there were no significant differences noted with sensitivity analysis.

Outcomes

Pain Relief

NRS scores are shown in Table 4. At 12 months, 73% of Group I participants and 70% of Group II participant showed significant pain relief. However, the proportion

Table 1. Baseline demographic characteristics.

		Group 1 (30)	Group II (30)	P value
Gender	Male	30% (9)	43% (13)	0.284
	Female	70% (21)	57% (17)	
Age	Mean ± SD	49.9 ± 8.5	49.7 ± 8.9	0.918
Weight	Mean ± SD	196.0 ± 54.2	170.7 ± 32.7	0.032
Height	Mean ± SD	66.5 ± 4.5	65.9 ± 3.7	0.617
Duration of pain (months)	Mean ± SD	115.2 ± 89.9	94.3 ± 77.4	0.338
Onset of the pain	Gradual	60% (18)	53% (16)	0.602
	Injury	40% (12)	47% (14)	
Pain ratio	Neck Pain only	18% (5)	11% (3)	0.531
	Neck worse than Upper extremity	68% (19)	54% (15)	
	Upper extremity worse than Neck	7% (2)	3% (1)	
	Both equal	7% (2)	32% (9)	
Neck Pain Distribution	Right	10% (3)	17% (5)	0.467
	Left	20% (6)	10% (3)	
	Bilateral	70% (21)	73% (22)	
Numeric rating score	Mean ± SD	7.9 ± 0.8	8.0 ± 0.9	0.762
Neck Disability Index	Mean ± SD	29.2 ± 5.2	29.2 ± 5.8	0.981

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

Group	Severe					Moderate					Mild				
	C3/4	C4/5	C5/6	C6/7	C7/T1	C3/4	C4/5	C5/6	C6/7	C7/T1	C3/4	C4/5	C5/6	C6/7	C7/T1
Primary*															
I	0	1	3	1	0	2	3	7	6	0	1	6	7	6	0
II	1	2	4	1	0	1	2	8	4	0	1	3	7	4	0
Total	1	3	7	2	0	3	5	15	10	0	2	9	14	10	0
Secondary															
I	0	0	0	0	0	0	0	0	1	0	2	2	1	0	0
II	0	0	0	0	0	0	0	0	0	0	1	0	1	1	0
Total	0	0	0	0	0	0	0	0	1	0	3	2	2	1	0

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

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

	Group I (30)	Group II (30)	Total
One Level	16	19	35
Two Levels	11	11	22
Three Levels	1	0	1
Four Levels	2	0	2

Table 4. *Mean pain relief of NRS scores and proportion of patients with significant pain relief (≥ 50%).*

Numeric Rating Score	Group I (30)	Group II (30)	*P* value
	Mean ± SD	Mean ± SD	
Baseline	7.9 ± 0.8	8.0 ± 0.9	0.862
3 months	3.7* ± 1.2 (87%)	3.5* ± 0.9 (87%)	0.625
6 months	3.4 * ± 0.9 (90%)	3.7* ± 1.0 (80%)	0.353
12 months	3.6* ± 1.1 (73%)	3.8* ± 1.2 (70%)	0.434

Percentages in parentheses indicate proportion of participants with significant relief (≥ 50% reduction in Numeric Rating Score from baseline)
* indicates significant difference with baseline values (P < 0.001)

Table 5. *Illustration of functional assessment scores by Neck Disability Index and proportion of patients with significant improvement (≥ 50%).*

Neck Disability Index	Group I (30)	Group II (30)	*P* value
	Mean ± SD	Mean ± SD	
Baseline	29.2 ± 5.2	29.2 ± 5.8	0.981
3 months	15.1* ± 5.8 (77%)	13.6* ± 3.8 (87%)	0.219
6 months	13.2* ± 4.8 (87%)	13.5* ± 4.6 (83%)	0.826
12 months	13.2* ± 5.4 (77%)	13.9* ± 4.5 (70%)	0.824

Percentages in parenthesis indicate proportion of patients with significant improvement with NDI scores from baseline (≥ 50%).
* indicates significant difference with baseline values (P < 0.001)

of participants in the successful categories reporting significant pain relief was 76% in Group I and 77% in Group II.

Functional Assessment

Table 5 shows functional assessment evaluated by NDI. Significant improvement was shown in both groups at 12 months: 77% in Group I and 70% in Group II. When further separated into failed and successful categories, the successful categories showed improvement in 79% of Group I and 77% of Group II.

Pain Relief and Functional Improvement

The proportion of participants with significant changes in pain and function are shown in Fig. 2. At 12 months, the changes are 73% in Group I and 70% in Group II. When successful categories are examined, there was improvement of 76% in Group I and 77% in Group II.

Employment Characteristics

Table 6 demonstrates employment characteristics in both groups.

Opioid Intake

Table 7 illustrates opioid intake characteristics.

Therapeutic Procedural Characteristics

Therapeutic procedural characteristics are illustrated in Table 8. Epidural entry was as follows: 10% between C5 and C6, 52% between C6 and C7, and 38% between C7 and T1 vertebral interspaces.

Average relief per year was 40.8 ± 16.3 weeks in Group I and 30.4 ± 16.1 weeks in Group II. The average number of injections per year was 3.7 ± 1.2 in Group I and 3.6 ± 1.2 in Group II. However, when patients were separated into successful and failed groups, the average number of injections per year was 3.8 ± 1.1 in Group I and 3.6 ± 1.2 in Group II in the successful group, with total relief of 42.2 ± 14.7 weeks in Group I and 34.3 ± 13.4 weeks in Group II with significant difference.

If a patient's relief lasted at least 3 weeks with 2 initial injections, then it was considered successful; if not, then it was considered a failure.

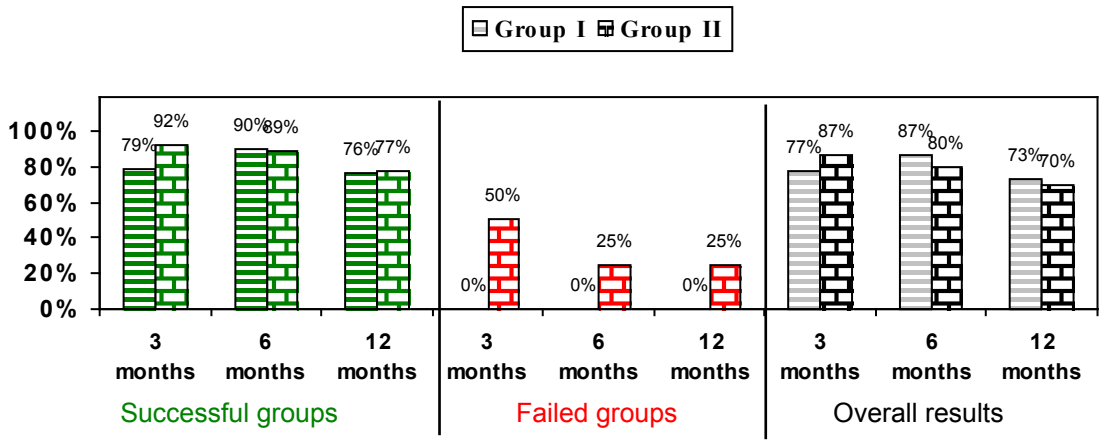

Fig. 2. *Illustration of reduction (at least 50%) in average pain and Neck Disability Index from baseline.*

Table 6. *Employment characteristics.*

Employment status	Group I (30)		Group II (30)	
	Baseline	12 months	Baseline	12 months
Employed part-time	0	0	0	1
Employed full-time	2	2	6	6
Unemployed (due to pain)	1	1	4	3
Not working	1	1	0	0
Eligible for employment	4	4	10	10
Total Employed	**2**	**2**	**6**	**7**
Housewife	22	22	18	18
Disabled	3	3	0	0
Retired	1	1	2	2
Total Number of Patients	**30**	**30**	**30**	

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

Opioid Intake (morphine equivalence mg)	Group I (30)	Group II (30)	*P* value
	Mean ± SD	Mean ± SD	
Baseline	51.37 ± 31.30	66.07 ± 72.62	0.313
3 months	45.63 ± 38.29	49.03* ± 70.40	0.817
6 months	45.13 ± 38.40	48.70* ± 70.52	0.809
12 months	46.13 ± 37.56	48.70* ± 70.52	0.861

* indicates significant difference with baseline values ($P < 0.001$)

Changes in Weight

Even though the 2 groups had a significant weight difference from each other at baseline, Table 9 illustrates that neither group showed a change in body weight from baseline.

Adverse Events

Two subarachnoid punctures, one intravascular entry and one report of soreness lasting one week were reported from the 214 procedures performed. No postoperative headache was reported in both patients after subarachnoid puncture.

Table 8. *Therapeutic procedural characteristics with procedural frequency, average relief per procedure, and average total relief in weeks over a period of one year.*

	Successful Patients		Failed Patients		Combined	
	Group I (29)	Group II (26)	Group I (1)	Group II (4)	Group I (30)	Group II (30)
1st procedure relief	7.1* ± 5.5 (29)	4.5 ± 3.8 (26)	0 (1)	1.6 ± 2.3 (4)	6.8* ± 5.6 (30)	4.1 ± 3.7 (30)
2nd procedure relief	11.6 ± 7.9 (28)	8.4 ± 2.9 (24)	-	1 ± 1.2 (4)	11.6* ± 7.9 (28)	7.4 ± 3.8 (28)
3rd procedure relief	13.6 ± 9.1 (25)	13.4 ± 5.1 (22)	-	10 (1)	13.6 ± 9.1 (25)	13.2 ± 5.1 (23)
4th procedure relief	12.9 ± 0.9 (20)	12.8 ± 1.8 (16)	-	-	12.9 ± 0.9 (20)	12.8 ± 1.8 (16)
5th procedure relief	12.4 ± 1.5 (7)	12.7 ± 0.8 (6)	-	-	12.4 ± 1.5 (7)	12.7 ± 0.8 (6)
Number of procedures per year	3.8 ± 1.1	3.6 ± 1.2	1	2.2 ± 0.5	3.7 ± 1.2	3.6 ± 1.2
Average relief per procedure	11.7 ± 5.5	9.6 ± 2.6	0	2.0 ± 1.9	11.3* ± 5.8	8.6 ± 3.6
Average relief per procedure after initial 2 procedures	13.7 ± 8.7	13.8 ± 4.7	-	10	13.7 ± 8.7	13.6 ± 4.7
Total relief per year (weeks)	42.2* ± 14.7	34.3 ± 13.4	0	5.0 ± 5.7	40.8* ± 16.3	30.4 ± 16.1

Table 9. *Characteristics of changes in weight.*

Weight (lbs)	Group I (30)	Group II (30)	*P* value
	Mean ± SD	Mean ± SD	
Weight at beginning	196.0 ± 54.2	170.7 ± 32.7	**0.032**
Weight at one year	190.7 ± 54.3	169.8 ± 30.4	0.070
Change	-5.3 ± 10.6	-0.9 ± 6.8	0.060
Lost weight	63%	47%	0.328
No change	17%	17%	
Gained weight	20%	36%	

Discussion

The fluoroscopic epidural injections in cervical spinal stenosis evaluated by randomized, double-blind, controlled trial showed significant pain relief in 73% in Group I and 70% in Group II with functional status improvement in 77% in Group I and 70% in Group II. The study also showed decrease in opioid usage. However, this study's results show no significant differences in pain relief or functional status whether patients received injections with steroids or without steroids. Specific data are illustrated in the tables above.

Cervical epidural injections are quite common, but systematic reviews are limited (14). There is one Cochrane review of medicinal and injection therapies for mechanical neck disorders (37). Benyamin et al (1) looked at the randomized evaluations included in the evidence synthesis (41-43). Their conclusions were that that positive results were shown for short-term relief in all 3 studies; positive results for long-term relief were shown in 2 studies, and the results of long-term relief were not available for one study (43). Short-term relief was defined as 6 months and long-term relief was defined as more than 6 months. Manchikanti et al, in 2 studies (51,52) evaluating the role of cervical epidural injections with or without steroids in patients with axial neck pain or disc herniation, showed significant improvement in physical and functional status in approximately 70% to 80% of the patients. But interlaminar epidural injections of local anesthetic with or without steroids do not provide long-term relief for patients with cervical spinal stenosis as shown in the present study. However, if patient evaluation is done appropriately and repeat injections are performed judiciously, long term relief can be achieved. The study has illustrated an average of 9.6 to 13.8 weeks of relief. Similar results have been shown for cervical epidurals using the same methodology for disc herniation (14), axial pain without disc herniation or facet joint pain (25), or cer-

vical post-surgery syndrome (55). The same is true for caudal and lumbar interlaminar epidurals ifor disc herniation, discogenic pain without disc herniation, spinal stenosis, and post surgery syndrome (51-54).

This study provides an understanding of the procedure's effectiveness for successful and failed categories in the two groups. Our results are generalizable for interventional pain management settings. It is also the first such study performed in an American private practice and that used fluoroscopy. Active control studies, such as the present one, measure effectiveness rather than efficacy like an explanatory trial, thus providing useful data (1,17-20,31,32,62-64). Such an active control design compares 2 commonly used therapies, rather than just an existence of effect or absolute effect size (65). Another difference in this study are the repeat injections given based on an increase in pain and functional status decline, rather than the normal routine of 3 injections or limiting the number of procedures.

The lack of a placebo group is a limitation for this study, but having a placebo group for interventional procedures in studies done in the United States is difficult (43,66-71). Unless the same methodology is used, along with fluoroscopic guidance, the results might not apply to the general patient population. Despite these caveats, this study does help shed light on whether steroids should be used with local anesthetic in injections .Corticosteroids appear to make no difference in a patient's improvement for managing chronic neck pain of spinal stenosis. There were differences in weight, but failed to influence results.

The mechanism of the action of steroids and local anesthetic has been described (43,72-92). There is also emerging evidence that local anesthetics may be equally as effective as steroids in managing low back and neck pain without disc herniation and also pain of facet joint origin (50-57,76-85).

Multiple complications also have been described with cervical epidural injections, including infection, bleeding, neural trauma, etc. (1,93-98); however, none were observed in this evaluation except 2 cases of subarachnoid puncture without further side effects.

Conclusion

This randomized, double-blind, controlled trial of cervical interlaminar epidural injections shows a 71.5% rate of effectiveness in pain reduction and functional status improvement for patients with chronic function-limiting neck pain and upper extremity pain secondary to central spinal stenosis.

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