Randomized Trial

Preliminary Results of a Randomized, Equivalence Trial of Fluoroscopic Caudal Epidural Injections in Managing Chronic Low Back Pain: Part 2 — Disc Herniation and Radiculitis

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Background: The pathophysiology of lumbar radicular pain is a subject of ongoing research. The prevalence of sciatica or radiculitis ranges from 1.2% to 43%. Epidural injections are one of the most commonly performed interventions in the United States in managing chronic low back and lower extremity pain secondary to disc herniation and radiculitis. There is a paucity of evidence with contemporary methodology used in performing epidural injections under fluoroscopy and based on pain relief and functional status improvement.

Study Design: A randomized, double-blind, equivalence trial.

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

Objective: To evaluate the effectiveness of caudal epidural injections with or without steroids in managing chronic low back and lower extremity pain secondary to disc herniation or radiculitis in providing effective and long-lasting pain relief and evaluate the differences between local anesthetic with or without steroids.

Methods: Patients were assigned to one of 2 groups; Group I patients received caudal epidural injections with an injection 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. Randomization was performed by computer-generated random allocations sequence by simple randomization.

Outcomes Assessment: Multiple outcome measures were utilized which included the Numeric Rating Scale (NRS), the Oswestry Disability Index 2.0 (ODI), employment status, and opioid intake with assessment at 3 months, 6 months, and 12 months post-treatment.

Significant pain relief was defined as 50% or more, whereas significant improvement in disability score was defined as a reduction of 40% or more.

Results: The percentage of patients with significant pain relief of 50% or greater at 12 months was 79% in Group I and 81% in Group II. Reduction of Oswestry scores of at least 40% was seen in 83% of the patients in Group I and 91% in Group II.

The overall average procedures per year were 3.9 ± 1.26 in Group I and 3.6 ± 1.08 in Group II with an average total relief per year of 35.2 ± 17.18 weeks in Group I and 35.9 ± 15.34 weeks in Group II over a period of 52 weeks.

Limitations: The results of this study are limited by lack of a placebo group and a preliminary report of 42 patients in each group.

Conclusion: Caudal epidural injections with or without steroids may be effective in patients with disc herniation or radiculitis with between 79% to 91% of patients showing significant pain relief and improvement in functional status.

Key words: Chronic low back pain, disc herniation, radiculitis, lower extremity pain, caudal epidural injections, epidural steroids, local anesthetic
CLINICAL TRIAL: NCT00370799

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Lumbosacral radicular syndrome is known by a range of terms in the literature, such as "sciatica," "radiculitis," "radiculopathy," "nerve root pain," and "nerve root entrapment," or "irritation" (1). Radicular pain is readily recognized in most cases in clinical practice in low back pain. It is generally defined as pain radiating to the leg, normally below the knee and into the foot and toes. The first to create widespread interest in the disc as a source of radicular pain in American literature were Mixter and Barr (2) with their 1934 hallmark description of the herniated nucleus pulposus. However, the pathophysiology of lumbar radicular pain is a subject of ongoing research and controversy with only a limited causative role for disc herniation and radiculitis, with non-specific or discogenic and facet joint pain assuming major roles (3-11). The pathophysiology of radicular pain assumes not only a mechanical component, but also multiple other factors including inflammation of the compressed nerve root, vascular compromise, and neurotoxicity (12-23). Konstantinou and Dunn (1) in a review of epidemiological studies and prevalence estimates of sciatica assessed the studies on sciatica prevalence and reported prevalence ranging from 1.2% to 43%. They described that the wide variation may be due to differences in definitions, methods of data collection, and perhaps populations studied.

Epidural injections for managing chronic pain are one of the most commonly performed interventions in the United States (9,24-31). The literature on the effectiveness of epidural steroid injections is mixed (9,24,28-31). The caudal epidural procedure is one of the 3 approaches available to access the lumbar epidural space in addition to interlaminar and transforaminal approaches. While there are multiple systematic reviews and other documents, only a few studies (9,24,29) have evaluated the effectiveness of epidural injections by separating the route of administration (caudal, interlaminar, and transforaminal). These evaluations showed moderate to strong evidence for caudal epidural injections in managing nerve root pain. Variations in results are explained on the basis of multiple issues, one of them being the lack of site-specific delivery of the local anesthetic and steroids when performed without fluoroscopy.

Reports of the effectiveness of epidural corticosteroids have varied from 18% to 90% (9,24,28-31). A common problem encountered with any epidural injection is inaccurate needle placement, which also results in inaccurate placement of the injectate (9,24,32,33). Thus, several authors have recommended that all epidural injections be performed using fluoroscopic guidance. In fact, multiple authors have evaluated accurate needle placement for caudal epidural injections with or without fluoroscopic guidance (9,24,32,33) showing incorrect needle placement in 20% to 38% of patients. Further, the underlying mechanism of action of epidural administered steroid and local anesthetic is not well understood. It is believed that the achieved neural blockade alters or interrupts nociceptive input, reflex mechanism of the afferent fibers, self-sustaining activity of the neurons, and the pattern of central neuronal activities (9,24,34,35). In addition, corticosteroids have been shown to reduce inflammation by inhibiting either the synthesis or release of a number of pro-inflammatory mediators and by causing a reversible local anesthetic effect (34-44). The evidence shows that the long-lasting effect may be obtained with local anesthetics with or without steroids (45-64). In fact, Tachihara et al (44) showed in rats that nerve root infiltration prevented mechanical allodynia; however, no additional benefit from using corticosteroid was identified, suggesting that corticosteroid may be unnecessary for nerve root blocks.

At present, there are no studies comparing the effectiveness of local anesthetic with or without steroid in managing lumbar radicular pain syndrome utilizing fluoroscopic visualization for delivery of the medication. Consequently, this study was undertaken to evaluate the effectiveness of caudal epidural injections with or without steroids in providing relief for chronic, function-limiting low back and lower extremity pain secondary to disc herniation and radiculitis in a randomized, double-blind, equivalency evaluation of 120 patients. This is a preliminary report of the one-year follow-up of 84 patients from a study scheduled for a 2-year follow-up with 120 patients.

Methods

The study was conducted in an interventional pain management practice, a specialty referral center, in a private practice setting in the United States. The study was performed based on Consolidated Standards of Reporting Trials (CONSORT) guidelines and an extension of the CONSORT statement reporting of non-inferiority and equivalence randomized trials (65-67). The study protocol was approved by the Institutional Review Board (IRB) and registered on the U.S. Clinical Trial Registry with an assigned number of NCT00370799.

Participants

Patients were assigned to one of 2 groups, with Group I patients receiving caudal epidural injections with injection 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. Each injection was a total volume of 10 mL (10 mL of lidocaine 0.5% or 9 mL of lidocaine with 1 mL of steroid), followed by 2 mL of 0.9% sodium chloride solution as a flush.

Interventions

All patients were provided with the IRB-approved protocol and the informed consent which described in detail all aspects of the study and withdraw process.

Pre-Enrollment Evaluation

The pre-enrollment evaluation included 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 by Oswestry Disability Index 2.0 (ODI).

Only patients with evidence of radiculitis or disc herniation based on historical, clinical, and radiological evaluations and with a duration of at least 6 months were included in the study.

Inclusion Criteria

Inclusion criteria were patients with disc herniation or radiculitis; patients who were 18 years of age; patients with a history of chronic function-limiting low back and lower extremity pain of at least 6 months duration; and patients who were competent to understand the study protocol and provide voluntary, written informed consent and participate in outcome measurements.

Exclusion criteria were previous lumbar surgery, radiculitis secondary to spinal stenosis without disc herniation, 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 steroid.

Description of Interventions

All caudal epidural procedures were performed by one physician in an ambulatory surgery setting, in a sterile operating room, under fluoroscopy, with patients in the prone position, under appropriate monitoring with intravenous access and sedation with midazolam and fentanyl. With sterile preparation, access to the epidural space was obtained, which was confirmed by injection of non-ionic contrast. Following this, injection of 10 mL of lidocaine hydrochloride 0.5% preservative free, or 9 mL of lidocaine mixed with 6 mg of betamethasone (either brand name or non-particulate) or 40 mg of methylprednisolone was carried out, followed by injection of 2 mL of 0.9% sodium chloride solution.

Repeat caudal epidural injections were provided based on the response to prior caudal epidural injections evaluated by improvement in physical and functional status. Further, repeat caudal epidural injections were performed only when increased levels of pain were reported with deteriorating relief below 50%.

Additional Interventions

All patients underwent the treatments as assigned. A patient was unblinded on request or if an emergency situation existed. If a patient required additional caudal epidural injections, these were provided based on the patient's response, either after unblinding or without unblinding. If the patient chose not to be unblinded, the prior treatment was repeated as assigned. However, if patients chose to be unblinded, they were offered either the assigned treatment or another treatment based on their response. If the patients were non-responsive and different treatments other than caudal epidural injections were required, they were considered to be withdrawn from the study, and no subsequent data were collected. However, patients who were non-responsive and continued with conservative management were followed without further epidural injections with medical management, unless they requested unblinding. In addition, all patients who were lost to follow-up were considered withdrawn. If patients were unavailable for follow-up they were considered as lost-to-follow-up.

Co-Interventions

Most patients were receiving opioids and non-opioid analgesics, adjuvant analgesics, and some were involved in a therapeutic exercise program. If patients were improving significantly and the medical necessity for these drugs was lacking, medications were stopped or dosages were decreased. In addition, dos-

ages were also increased, based on medical necessity. All patients continued previously directed exercise programs, as well as their work. Thus, in this study, there was no specific physical therapy, occupational therapy, bracing, or other interventions offered other than the study intervention.

Objectives

The study was designed to evaluate the effectiveness of caudal epidural injections with or without steroids in managing chronic low back and lower extremity pain secondary to disc herniation or radiculitis in providing effective and long-lasting pain relief and evaluate the differences between local anesthetic with or without steroids.

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 months, 6 months, and 12 months post-treatment. NRS represented no pain with a 0 and the worst pain imaginable with a 10. The ODI was utilized for functional assessment. The value and validity of the NRS and ODI have been reported (67,68). Thresholds for the minimum clinical important difference for ODI varied from a 4 to 15 point change from a total score of 50. Significant pain relief was established as 50% or more reduction in NRS from baseline, whereas significant improvement and function was described as at least a 40% reduction in ODI (61-63).

Based on the dosage frequency and schedule of the drug, the opioid intake was converted into morphine equivalents (69).

Employment and work status were determined based on employability at the time of enrollment rather than including all the patients in the study as employable. Employment and work status were classified into multiple categories such as employable, housewife with no desire to work outside the home, retired, or over the age 65. Patients who were unemployed due to pain or employed but on sick leave or laid off were considered as employable.

The epidurals were determined to be successful if a patient obtained consistent relief with the first and second procedures of at least one and 3 weeks and the relief with the second injection outlasted the first injection. All others were considered to be failures.

Sample Size

Sample size is calculated based on significant pain relief. Considering a 0.05 two-sided significance level, a power of 80%, and an allocation ratio of 1:1, 18 patients in each group were estimated (70) allowing for 10% attrition/non-compliance rate, 40 subjects were required.

Previous studies of interventional techniques identified 50 to 60 patients as acceptable (61-63,71).

Randomization

From a total of 120 patients, 60 patients were randomly assigned into each group.

Sequence Generation

Randomization was performed by computer-generated random allocations sequence by simple randomization.

Allocation Concealment

The operating room nurse assisting with the procedure randomized the patients and prepared the drugs appropriately.

Implementation

Participants were invited to enroll in the study if they met inclusion criteria. One of the 3 nurses assigned as coordinators of the study enrolled the participants and assigned participants to their respective groups.

Blinding (Masking)

Participants and those administering the interventions were blinded to group assignment. The blinding was assured by mixing the patients with other patients receiving routine treatment and not informing the physician performing the procedure of the inclusion of the patients in the study. All the patients for one-year follow-up were selected by the statistician not participating in provision of patient care. The unblinding results were not disclosed to either the treating physician or other participants or patients. Thus, the nature of blinding was not interrupted.

Statistical Methods

Statistical analysis included the chi-squared statistic, Fisher's exact test, t-test, and paired t-test. Results were considered statistically significant if the *P* value was less than 0.05.

Chi-squared statistic was used to test the differences in proportions. Fisher's exact test was used wherever the expected value was less than 5; 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 months, 6 months, and 12 months. For comparison of mean scores between groups, t-test was performed.

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 and no other data were available.

Results

Participant Flow

Figure 1 illustrates the participant flow.

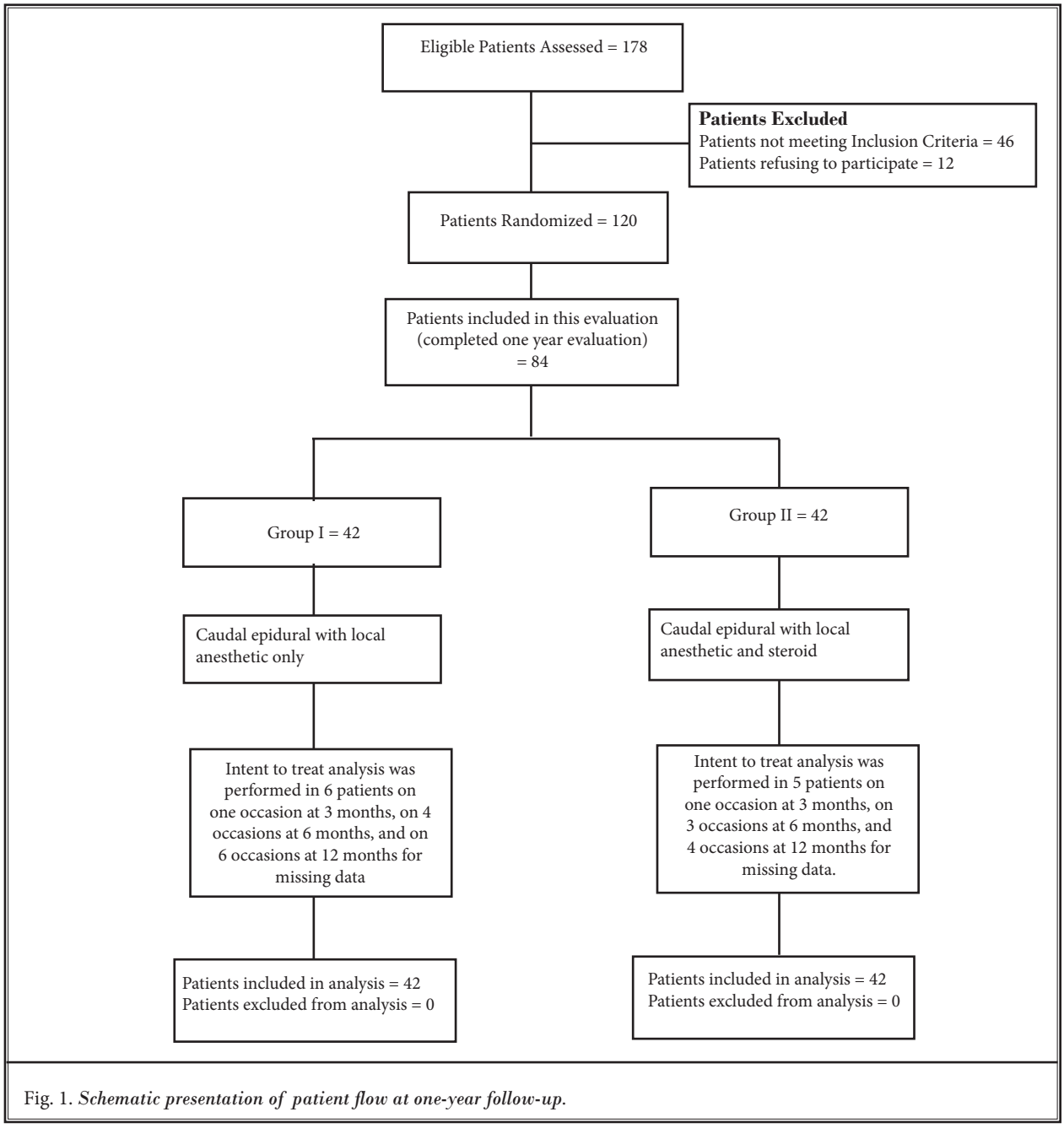


Fig. 1. *Schematic presentation of patient flow at one-year follow-up.*

Recruitment

The recruitment period lasted from January 2007 to August 2008.

Baseline Data

Baseline demographic and clinical characteristics of each group are illustrated in Table 1. There were significant differences noted between the groups with mean weight; however, no other differences were noted.

Analysis of Data

Numbers Analyzed

A schematic illustration of patient flow is provided in Fig. 1. The study period for one-year follow-up lasted from January 2007 to August 2008 with completion of one-year follow-up of 84 patients with 42 patients in each group. In Group II, 17 patients received non-particulate Celestone, 11 received brand-name Celestone, and 14 received depomethylprednisolone. The data were available in the majority of the included patients. Intent-to-treat analysis was performed due to non-available data on 11 occasions in Group I on a total of 6 patients, and on 8 occasions on 5 patients in Group II. Based on the number of treatments provided, lack of follow-up was found in 11 of 126 occasions in Group I (8.7%) or 6 of 42 patients (14.3%); whereas it was 8 of 126 occasions (6.3%) in Group II with 5 of 42 patients (12%) at least one time.

Outcomes

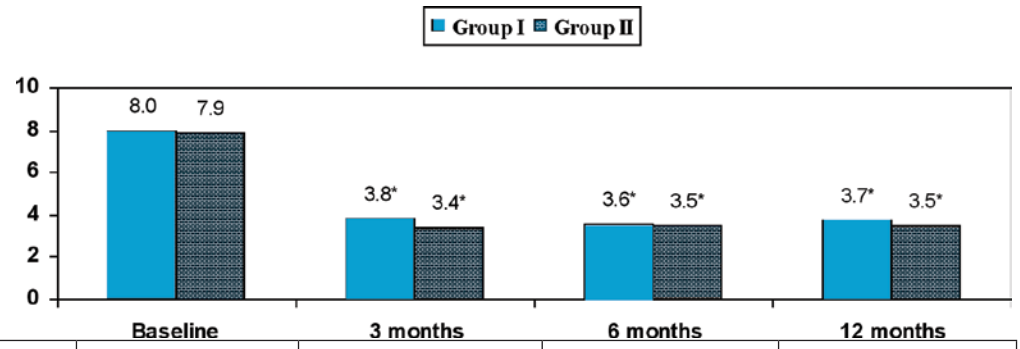
Pain Relief

Figure 2 illustrates the NRS scores. Pain scores changed significantly from baseline, at 3 months, 6 months, and 12 months in all groups, with no significant differences between the groups or follow-up periods.

The proportion of patients with significant pain relief of 50% or greater are illustrated in Fig. 3 with 79% in Group I and 81% in Group II at 12 months. There were no significant differences between the groups or from the 3-month to 6-month to 12-month outcomes.

Table 1. *Baseline demographic and clinical characteristics of participants.*

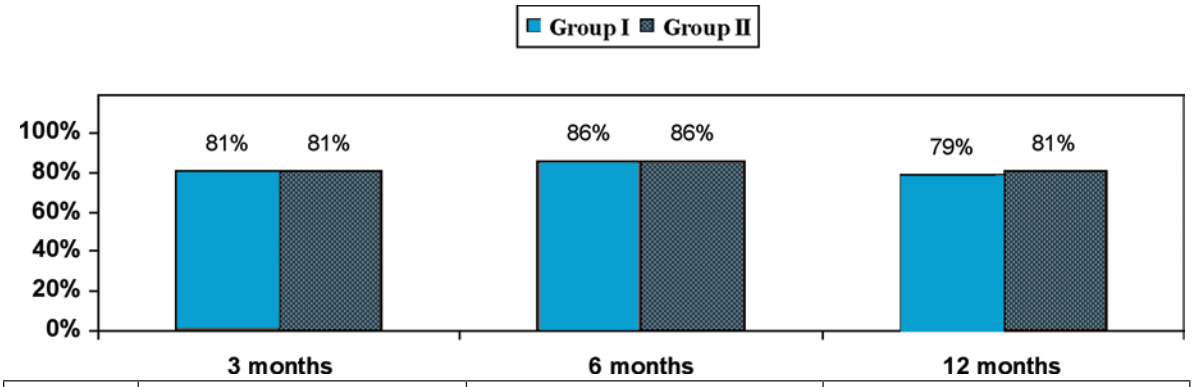
		Group I (n=42)	Group II (n=42)	*P* value
Gender	Male	33% (14)	33% (14)	1.000
	Female	67% (28)	67% (28)	
Age	Mean ± SD	48.6 ± 13.88	45.5 ± 15.99	0.350
Weight	Mean ± SD	205 ± 53.11	181 ± 44.02	0.027
Height	Mean ± SD	66.3 ± 3.59	66.2 ± 3.80	0.906
Duration of Pain	Mean ± SD	91.1 ± 86.71	93.8 ± 91.48	0.890
Onset of the Pain	Gradual	64% (27)	48% (20)	0.187
	Injury	36% (15)	52% (22)	
Low Back Pain Distribution	Bilateral	67% (28)	69% (29)	0.897
	Left or right	33% (14)	31% (13)	
Leg Pain Distribution	Bilateral	31% (13)	40% (17)	0.640
	Left or right	69% (29)	60% (25)	
Numeric Pain Rating Score	Mean ± SD	8.0 ± 0.81	7.9 ± 0.96	0.713
Oswestry Disability Index	Mean ± SD	28.6 ± 4.59	28.5 ± 4.37	0.884



Group I (n=42)	8.0 ± 0.81	3.8* ± 1.55	3.6* ± 1.50	3.7* ± 1.39
Group II (n=42)	7.9 ± 0.96	3.4* ± 1.69	3.5* ± 1.70	3.5* ± 1.84
P value	0.713	0.205	0.892	0.548

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

Fig. 2. *Illustration of pain relief characteristics (mean ± SD).*

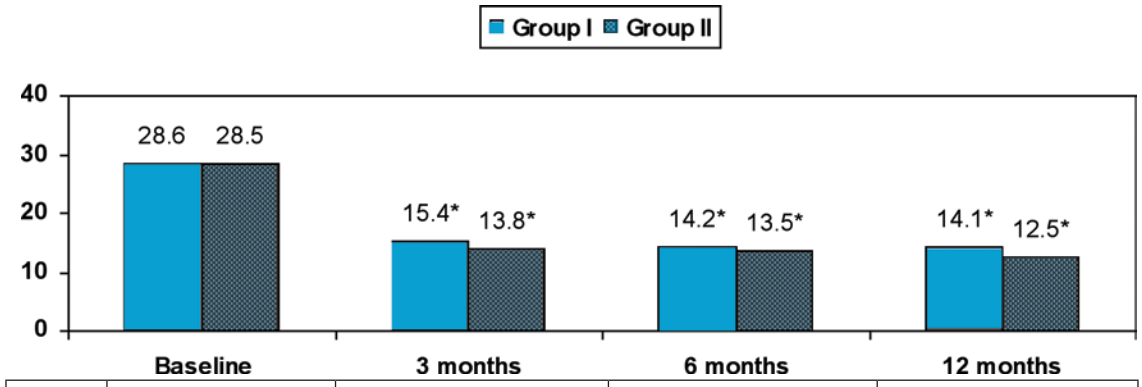


Group I (n=42)	81% (34)	86% (36)	79% (33)
Group II (n=42)	81% (34)	86% (36)	81% (34)
P value	1.000	1.000	1.000

Fig. 3. *Illustration of significant pain relief (≥ 50% reduction in Numeric Rating Score from baseline).*

Functional Assessment

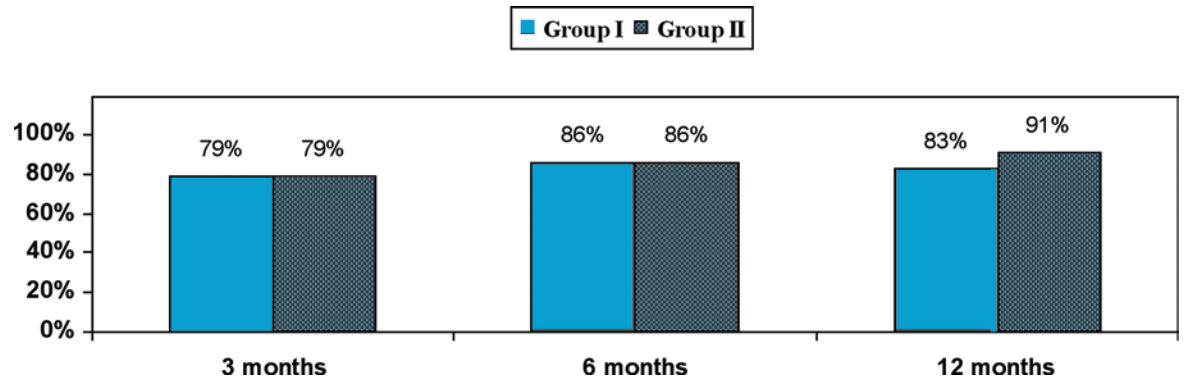
Functional assessment results assessed by the ODI are illustrated in Fig. 4. Significant improvement was seen in the functional status in both groups from baseline to one year. Reduction of Oswestry scores of at least 40% was seen in 83% (Group I) and 91% (Group II) of the patients as shown in Fig. 5. There were no significant differences between the groups or during follow-up periods.



	Baseline	3 months	6 months	12 months
Group I (n=42)	28.6 ± 4.59	15.4* ± 6.77	14.2* ± 6.73	14.1* ± 6.89
Group II (n=42)	28.5 ± 4.37	13.8* ± 6.29	13.5* ± 6.65	12.5* ± 6.38
P value	0.884	0.253	0.637	0.289

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

Fig. 4. *Illustration of average Oswestry Disability Index for functional assessment (scale 0–50%).*



	3 months	6 months	12 months
Group I (n=42)	79% (33)	86% (36)	83% (35)
Group II (n=42)	79% (33)	86% (36)	91% (38)
P value	1.000	1.000	0.520

Fig. 5. *Illustration of reduction (≥40%) of Oswestry Disability Index from baseline.*

Table 2. *Employment characteristics.*

Employment status	Group I		Group II	
	Baseline	12 months	Baseline	12 months
Employed part-time	0	1	4	4
Employed full-time	6	9	5	12
Unemployed/laid off/sick	6	3	8	1
Total Employed	6 (50%)	10 (83%)	9 (53%)	16 (94%*)
Eligible for employment	**12**	**12**	**17**	**17**
Housewife with no desire to work outside	6	5	1	1
Disabled	20	20	18	18
Over 65 year of age	4	4	6	6
Total Number of Patients	**42**	**42**	**42**	**42**

* indicates significant difference with baseline values ($P< 0.05$).

Table 3. *Narcotic intake based on morphine equivalents in milligrams.*

Opioid intake	Group I (n=42)	Group II (n=42)	*P* value
	Mean ± SD	Mean ± SD	
Baseline	48.7 ± 45.26	45.6 ± 45.63	0.763
3 months	28.7# ± 15.47	27.4# ± 20.36	0.732
6 months	28.5# ± 15.68	26.7# ± 20.79	0.649
12 months	28.6# ± 15.62	27.2# ± 20.79	0.741

# indicates significant difference with baseline values ($P < 0.05$).

Employment Characteristics

Table 2 demonstrates employment characteristics in both groups. At baseline, there were 12 patients eligible for employment in Group I and 17 patients eligible in Group II, whereas the number of patients eligible for employment remained the same at 12 months in both groups. Of these, there were 10 patients employed in Group I and 16 in Group II.

The employment showed significant increase in Group II from 9 (53%) employed to 16 (94%) employed.

Opioid Intake

Table 3 illustrates opioid intake between both groups at baseline and at 12 months that showed no significant change in intake of opioids. However, opioid intake significantly decreased from their baseline opioid intake in both groups at 3, 6, and 12 months.

Therapeutic Procedural Characteristics

Therapeutic procedural characteristics with average pain relief per procedure are illustrated in Table 4. Average relief per year of 35.2 ± 17.18 weeks in Group I and 35.9 ± 15.34 weeks in Group II with no significant differences. The total number of injections per year were 3.9 ± 1.26 in Group I and 3.6 ± 1.08 in Group II. However, when patients were separated into successful and failed groups, the total number of injections per year was 4.1 ± 1.13 in Group I and 3.6 ± 1.05 in Group II in the successful group, whereas it was 2.9 ± 1.46 for Group I and 3.7 ± 1.37 for Group II in the failed group. Total relief of 40.2 ± 12.14 weeks in successful group in Group I and 39.1 ± 12.09 weeks in Group II. In contrast, the relief was 10.4 ± 17.09 and 16.8 ± 20.01 weeks in failed group.

Epidurals were considered to be successful if a patient obtained consistent relief with the first and sec-

Table 4. *Illustration of procedural characteristics with procedural frequency, average relief per procedure, and average total relief in weeks over a period of one year.*

	Successful group		Failed group		Overall	
	Group I (n=35)	Group II (n=36)	Group I (n=7)	Group II (n=6)	Group I (n=42)	Group II (n=42)
1st injection relief	6.0 ± 6.45 (35)	7.1 ± 6.65 (36)	0.7 ± 1.11 (7)	0.17 ± 0.41 (6)	5.1 ± 6.22 (42)	6.1 ± 6.62 (42)
2nd injection relief	9.5 ± 5.35 (34)	13.9 ± 17.65 (35)	2.3 ± 4.32 (6)	1.7 ± 2.73 (6)	8.4 ± 5.8 (40)	12.1 ± 16.89 (41)
3rd injection relief	12.8 ± 5.72 (32)	13.8 ± 12.96 (31)	5.7 ± 5.03 (3)	7.0 ± 6.38 (4)	12.2 ± 5.96 (35)	13.1 ± 12.51 (35)
4th injection relief	12.0 ± 2.79 (24)	12.3 ± 2.92 (22)	8.0 ± 7.00 (3)	4.8 ± 6.18 (4)	11.6 ± 3.51 (27)	11.2 ± 4.41 (26)
5th injection relief	11.8 ± 2.07 (17)	13.0 ± 0.0 (7)	13.0 (1)	21.5 ± 6.36 (2)	11.9 ± 2.02 (18)	14.9 ± 4.37 (9)
Number of injections per year	4.1 ± 1.13 (35)	3.6 ± 1.05 (36)	2.9 ± 1.46 (7)	3.7 ± 1.37 (6)	3.9 ± 1.26 (42)	3.6 ± 1.08 (42)
Total relief per year (weeks)	40.2 ± 12.14 (35)	39.1 ± 12.09 (36)	10.4 ± 17.91 (7)	16.8 ± 20.01 (6)	35.2 ± 17.18 (42)	35.9 ± 15.34 (42)

Table 5. *Characteristic weight monitoring.*

Weight (lbs)	Group I (n=42)	Group II (n=42)	*P* value
	Mean ± SD	Mean ± SD	
Initial weight	204.8 ± 53.11	180.7± 44.0	0.027
Weight at one year	198.7 ± 59.98	178.7 ± 44.35	0.055
Change	-6.1 ± 11.04	-2.0 ± 8.13	0.061
Participants with weight loss	57% (24)	64% (27)	0.648
Participants without change	19% (8)	12% (5)	
Participants with weight gain	24% (10)	24% (10)	

ond injections of at least 1 and 3 weeks and the relief with the second injection outlasted the first injection. All others were considered as failures.

Changes in Weight

There were no differences in change (gain or loss) in body weight from baseline in both groups (Table 5). At the same time, there were no differences based on weight, even though baseline characteristics (Table 1) showed Group I patients significantly more overweight than Group II patients.

Adverse Events

There were no major adverse events reported over a period of one year in 84 patients.

Discussion

The preliminary report of a one-year follow-up of a randomized, equivalence trial of 84 patients demonstrated significant pain relief (≥ 50%) in 79% to 81% of the patients with significant improvement in functional status with (40% or greater reduction in Oswestry scores) in 83% to 91% of the patients at the end

of one-year follow-up with no significant differences noted with or without steroids. The overall average procedures per year were 3.9 ± 1.26 in Group I and 3.6 + 1.08 in Group II, with an average total relief per year of 35.2 ± 17.18 weeks for Group I and 35.9 ± 15.34 weeks for Group II, over a period of 52 weeks.

Opioid intake and employment also showed significant improvements. Opioid intake was significantly reduced in both groups along with the pain relief and improvement in functional status. Further, employment was significantly increased in Group II compared to baseline employment.

Despite widespread use and numerous publications there is significant controversy with regards to the medical necessity and indications for lumbar epidural injections (9,24-31). Multiple systematic reviews, guidelines, and other reviews have identified indications for caudal epidural injections in positive reports to treat radicular pain from herniated lumbar intervertebral discs and radiculitis. Manchikanti et al (29) in a reassessment of an evidence synthesis of occupational medicine practice guidelines, utilizing only randomized trials, with a definition of short-term relief of 6 months or less and long-term relief of longer than 6 months presented with evidence of Level I in managing pain secondary to disc herniation and radiculitis with caudal epidural injections (72-75). Of the randomized evaluations included in the evidence synthesis (72-75), 3 studies showed positive results for short-term relief of 6 months (72,74,75), whereas, both of the 2 studies evaluating the long-term relief showed positive results (73,75). As illustrated in the present study, caudal epidural injections with or without steroids do not provide long-term relief, even though long-term relief can be achieved by appropriate patient evaluation and judicious use of repeat injection therapy. This study has illustrated an average relief of 12–15 weeks of relief in the therapeutic phase after 2 initial injections. These results are similar to patients receiving caudal epidural injections with or without steroids without disc herniation or radiculitis and also without facet joint pain (76), but superior to patients suffering with spinal stenosis and post-surgery syndrome (77,78). Thus, the results of this randomized equivalency trial reinforce the previous findings with long-term follow-up.

Further, this study also provided insight into successful or failed groups based on the first 2 procedures. The patients in the successful group with good pain relief with the first and second procedures showed average relief from 39 to 40 weeks of 52 weeks with average number of procedures per year of 3.6 to 4.1. In contrast, in the failed group, the average relief per procedure was 5 to 12 weeks, with overall 10 to 17 weeks of relief in one year.

One of the advantages of this evaluation is its generalizability to interventional pain management settings. Further, this is the first study performed under fluoroscopic visualization in the United States and also as an equivalence trial, which is considered to be a practical clinical trial, providing more generalizability than a placebo control trial. Consequently, the results of this study may be applied to individual patients or groups that differ from those controlled in the placebo trials. Pragmatic or practical clinical trials (with an active control) measuring effectiveness are considered more appropriate than explanatory trials measuring efficacy (66,67,79-84). Pragmatic trials are best designed to provide the results of benefit of the treatment produced in routine clinical practice, in contrast to explanatory trials (placebo control) measuring efficacy. Utilizing an active control design, in this study, the evidence is based on head-to-head comparisons of clinically relevant alternatives used in routine clinical practice, which include local anesthetic with or without steroids. In contrast, a placebo control trial measures absolute effect size and shows the existence of effect. In contrast, the present design with active control shows not only the existence of effect, but also compares 2 commonly used therapies (84). This study is also different from other studies as we have utilized repeat caudal epidural injections based on the requirement that there be an with increase in pain and deterioration in functional status rather than routinely providing 3 injections or limiting to 3 procedures or limiting them even to only one or 2 procedures. Further, this study also has taken into consideration that the initial 2 procedures do not last for long periods of time and if the initial relief does not last more than one to 3 weeks the procedures do not provide long-term relief in patients as observed in the failed subjects.

The study may be criticized or considered as deficient due to the lack of a placebo group and preliminary analysis. However, there have been investigations in the past which utilized a placebo group. Further, conducting clinical trials with a placebo group is extremely difficult in the United States with interventional techniques. External validity also known as applicability, is the extent to which the results of

the study can be generalized to other circumstances and the general population, and is best provided with pragmatic or active control trials such as this one. The issue of a lack of a placebo group is addressed in pragmatic trials with a treatment response accounting for the total difference between 2 treatments, including both treatment as well as associated placebo effects, which provides the internal validity. This preliminary report may resolve to some extent the issue of local anesthetics with or without steroids in managing chronic function-limiting low back and lower extremity pain with disc herniation or radiculitis. These results describe a pattern of practice in the United States in an interventional pain management setting. Thus, the results may not be applicable in the general population unless the same methodology is utilized under fluoroscopy. In addition, generalizability of the findings of any study may only be feasible utilizing larger populations in multiple settings.

In addition, preliminary analysis is not a disadvantage. The sample size analysis showed a requirement of 26 patients per group, thus the inclusion of 42 patients in each group exceeds the sample size requirement.

While the mechanism of action of steroids and local anesthetic has been described (34-64), there is emerging evidence that local anesthetics may be equally as effective as steroids in managing low back pain without disc herniation and also pain of facet joint origin (56,58,61-63,76-78). It has been reported that multiple pathophysiologic mechanisms involved in chronic pain including noxious peripheral stimulation, excess nociception resulting in the sensitization of the pain pathways at several neuronal levels (45,85), and excess release of neurotransmitters causing complex central responses including hyperalgesia or wind-up (43), resulting in an increase in nociceptive sensitization of the nervous system (64,86), and phenotype changes which are also considered as part of the neuronal plasticity (64,86,87). Thus, there is evidence for long-term effect of either local anesthetics or steroids in managing radicular pain. Corticosteroid anti-inflammatory properties have been associated with the inhibition of prostaglandin synthesis and decreases in regional levels or inflammatory mediators such as interleukin-1, tumor necrosis factor, and phospholipase A2 (14-23,36-42,88-91). The present study along with previous studies (56,58,76-78) once again demonstrates the lack of a significant role for corticosteroids in managing chronic low back pain with or without lower extremity pain, and in this study specifically in patients with disc herniation and radiculitis. In addition, corticosteroids are also known to possess direct neurotoxic effects on peripheral nerve tissue unlike local anesthetics (35,92-94).

In summary, the evidence in this preliminary evaluation of a randomized equivalence trial demonstrates that caudal epidural injections in patients with disc herniation and radiculitis provides significant relief and these patients may be treated with caudal epidural injections with or without steroids, providing 12–14 weeks of relief with each procedure and requiring 3 to 4 episodes of treatment per year after the initial 2 procedures.

Conclusion

The assessment of preliminary results of this randomized, controlled, equivalence trial of caudal epidural injections in chronic function-limiting low back pain and lower extremity pain with disc herniation and radiculitis demonstrated the effectiveness in over 79% of the patients with improvement in functional status, requiring 3 to 4 procedures per year and providing almost 40 weeks of relief during a 52-week period in appropriately selected patients.

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