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Randomized Trial

Preliminary Results of a Randomized, Equivalence Trial of Fluoroscopic Caudal Epidural Injections in Managing Chronic Low Back Pain: Part 1 — Discogenic Pain without Disc Herniation or Radiculitis

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Background: Intervertebral discs, facet joints, ligaments, fascia, muscles, and nerve root dura have been described as tissues capable of transmitting pain in the low back. The pathophysiology of spinal radicular pain is the subject of ongoing research and controversy with discogenic pain assuming a major role as a cause of non-specific low back pain. Even though epidural injections are frequently administered in managing axial low back pain, the evidence is lacking.

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.

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

Methods: Patients were randomly assigned to one of 2 groups, Group I patients received caudal epidural injections with 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 allocation 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 reduction of 40% or more.

Results: Significant pain relief (≥ 50%) was demonstrated in 72% to 81% of patients and functional status improvement was demonstrated by a reduction of 40% in the ODI scores in 81% of the patients. The overall average procedures per year were 3.6 ± 1.05 in Group I and 3.9 ± 1.33 in Group II with an average total relief per year of 32.3 ± 16.93 weeks in Group I and 30.7 ± 17.94 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 36 patients in each group.

Conclusion: Caudal epidural injections with or without steroids may be effective in patients with chronic function-limiting low back pain without facet joint pain, disc herniation, and/or radiculitis in over 70% of the patients.

Key words: Chronic low back pain, caudal epidural injections, discogenic pain, disc herniation, radiculitis, local anesthetic, steroids, controlled comparative local anesthetic blocks, provocation discography
CLINICAL TRIAL: NCT00370799

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Kuslich et al (1) identified intervertebral discs, facet joints, ligaments, fascia, muscles, and nerve root dura as tissues capable of transmitting pain in the low back. The first to create widespread interest in the disc as a source of pain in American literature were Mixter and Barr (2) with their 1934 hallmark description of the herniated nucleus pulposus. However, soon after, the report of Mixter and Ayers (3) in 1935, demonstrated that radicular pain can occur without disc herniation. Subsequently, numerous investigators (4-13) have described pain syndromes emanating from lumbar intervertebral disc without mechanically compressing neural structures. The pathophysiology of spinal radicular pain is the subject of ongoing research and controversy and discogenic pain has assumed a major role as a cause of non-specific low back pain, beyond the more specific disc herniation.

Modern technology including magnetic resonance imaging (MRI), computed tomography (CT) axial scanning, neurophysiologic testing, and comprehensive physical examination with psychological evaluation, can identify the cause of low back pain in only 15% of patients in the absence of disc herniation and neurological deficit (14-17). However, utilizing controlled diagnostic blocks, the prevalence of pain due to internal disc disruption was reported to be 39% in patients suffering with chronic low back pain (6), whereas primary discogenic pain was reported in 26% (5) when no other cause was suspected. Further, facet joint pain has been shown to be present in 15% to 45% of patients (5,18-23), whereas sacroiliac joint pain has been established in 10% to 18.5% of the population (5,24). In a study by Manchikanti et al (5) of the relative contributions of various structures in patients with chronic low back pain who failed to respond to conservative modalities of treatments with lack of radiological evidence to indicate disc protrusion or radiculopathy, 40% of the patients were shown to have facet joint pain, 26% discogenic pain, 2% sacroiliac joint pain, and possibly 13% segmental dural/nerve root pain with lack of identification of cause in 19% of the patients. Consequently, approximately 58% of patients either with discogenic pain, segmental dural nerve root pain, or non-identifiable cause may respond to epidural injections.

Epidural injections for managing chronic low back pain are one of the most commonly performed interventions in the United States (25-27). Friedly et al (28) reported administration of epidural injections in 36% of patients with axial low back pain. However, there is no clinical evidence for the use of epidural injections in axial low back pain and most recommendations are limited to radicular pain with disc herniation (29-31) except for 2 observational studies utilizing caudal approach (32,33) and one utilizing interlaminar approach (34). Thus, epidural steroid injections are not only the most commonly used procedures in interventional pain management, but also the most contentious and misunderstood modality of treatment (13,29-31).

Multiple approaches available to access the epidural space in the lumbosacral spine include interlaminar, transforaminal, and caudal. The overall effectiveness of epidural steroid injections has been highly variable. The evidence for caudal epidural injections (13,29,30) is Level I in managing pain secondary to disc herniation and radiculitis, whereas in managing axial low back pain the evidence is limited.

Two prospective observational studies have shown significant improvement with caudal epidural injections with or without steroids in patients with chronic low back pain (32,33). Manchikanti et al (32) evaluated the effectiveness of caudal epidural injections in positive and negative chronic low back pain patients after they had failed to show evidence of facet joint pain. They studied 62 patients with the results showing that there was significant improvement in patients receiving caudal epidural injections, with a decrease in pain associated with improved physical, functional, and mental status, decreased opioid intake, and increased return to work. In another study, Manchikanti et al (33) evaluated 65 patients who underwent diagnostic facet joint nerve blocks utilizing controlled comparative local anesthetic block and were found to be negative for facet joint pain and other problems such as sacroiliac joint pain. The results showed that there was significant improvement in patients receiving caudal epidural injections, with a decrease in pain associated with improved physical, functional, and mental status along with return to work. Butterman (34) also evaluated the effect of spinal steroid injections for degenerative disc disease utilizing either interlaminar or transforaminal injections in patients with chronic low back pain of more than one year's duration in a prospective evaluation over a period of 4 years. They reported the effectiveness of epidural steroid injections in improving pain and function at 3 month follow-up. However, at subsequent follow-up periods, the success rate declined. In this study, 1–3 procedures were administered rather than repeating them based on the return of pain.

This study was undertaken to evaluate the role of caudal epidural injections in patients with chronic low back pain without disc herniation or radiculitis, and negative for facet joint pain by means of controlled comparative local anesthetic blocks. The study is designed to evaluate 120 patients. This preliminary report includes 72 patients completing one-year follow-up.

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 (35-37). 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 the withdrawal process.

Pre-Enrollment Evaluation

The pre-enrollment evaluation included the exclusion of facet joint pain by controlled comparative local anesthetic blocks. Additional information 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).

All patients without evidence of disc herniation or radiculitis, but with chronic low back pain were evaluated and included in the study. The diagnosis was based on controlled facet joint nerve blocks to exclude patients with lumbar facet joint pain which was suspected based on historical, clinical, and radiological evaluations. Only patients with non-specific low back pain with a duration of at least 6 months were included. Patients with disc herniation with or without radicular symptoms were excluded.

Inclusion Criteria

Inclusion criteria were a negative diagnosis of lumbar facet joint pain by means of controlled comparative local anesthetic blocks; patients over the age of 18 years; patients with a history of chronic function-limiting low back 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.

Inclusion criteria also included that there was no evidence of disc herniation and patients also had undergone and failed to show positive response to facet joint nerve blocks and also had failed to improve substantially with conservative management including but not limited to physical therapy, chiropractic manipulation, exercises, drug therapy, and bedrest.

Exclusion criteria were a positive response to controlled comparative local anesthetic blocks, previous lumbar surgery, 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

All patients were treated with controlled comparative local anesthetic facet joint nerve blocks. The process started with diagnostic facet joint nerve blocks with 0.5 mL of 1% lidocaine, followed by blockade of facet joint nerves with 0.25% bupivacaine on separate occasions. If they were lidocaine-positive, a response was considered negative, if pain relief lasted less than 2 hours following the lidocaine injection, and lasted less then 3 hours or less than the duration of relief with lidocaine when bupivacaine was used. Controlled, comparative local anesthetic blocks were also performed for sacroiliac joint pain.

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 response to previous injection, 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. Patients unavailable for follow-up were considered as lost-to-follow-up.

Co-Interventions

Most patients were receiving opioid 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, dosages 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 pain without disc herniation or radiculitis in providing effective and long-lasting pain relief and to evaluate the differences between local anesthetic with or without steroid.

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 (37,38). Thresholds for the minimum clinical important difference for the ODI varied from a 4 to 15 point change from a total score of 50. Significant pain relief was described as 50% or more reduction in NRS from baseline, whereas significant improvement and function was described as at least a 40% reduction in the ODI (39-41).

Based on the dosage frequency and schedule of the drug, the opioid intake was converted into morphine equivalents (42).

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

Sample Size

Sample size is calculated based on reduction of NRS. A minimal clinical difference change of 1.2 (d) was set from a previous study (33). With standard deviation (σ) of the NRS of 1.5, $\delta = d/\sigma$, $\delta = 0.80$, to achieve an alpha of 0.05 and beta of 0.20 with 80% power (43), it required 26 patients in each group of the trial, allowing for 10% attrition/non-compliance rate, 58 subjects were required.

Previous studies of interventional techniques have identified 50 to 60 patients as acceptable (39-41,44).

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 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 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.

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 no significant differences noted between the groups.

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 72 patients with 36 patients in each group. In Group II, 12 patients each received non-particulate Celestone, brand-name Celestone, or Depo-Medrol. The data were available in the majority of the included patients. Intent-to-treat analysis was performed due to non-available data on 10 occasions in Group I on a total of 7 patients, and on 5 occasions on 3 patients in Group II. Based on the number of treatments provided, lack of follow-up was found in 10 of 108 occasions (9.3%) in Group I or 7 of 36 patients (19.4%); whereas it was 5 of 108 (4.6%) occasions in Group II with 3 of 36 patients (8.3%) at least one time.

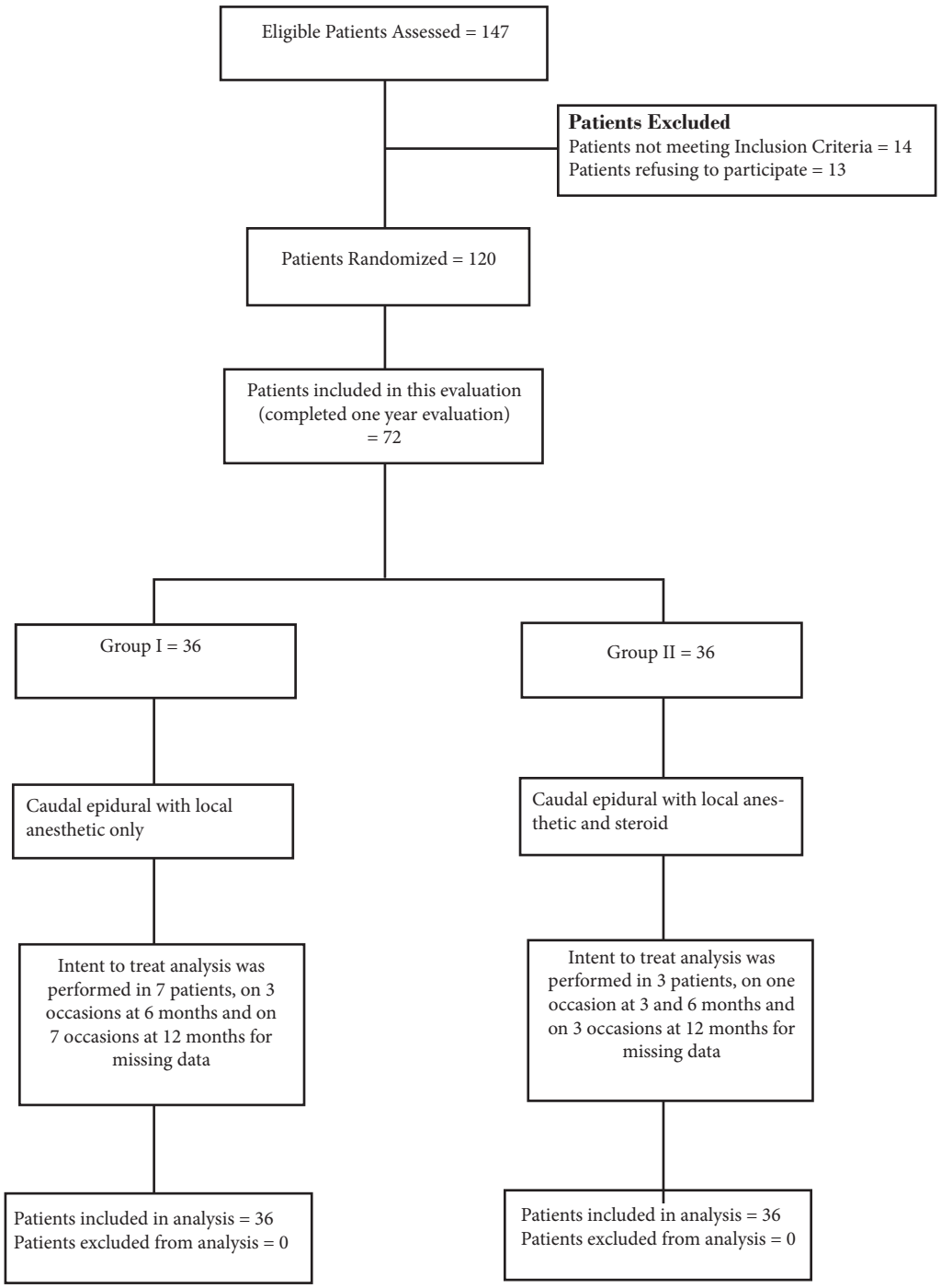
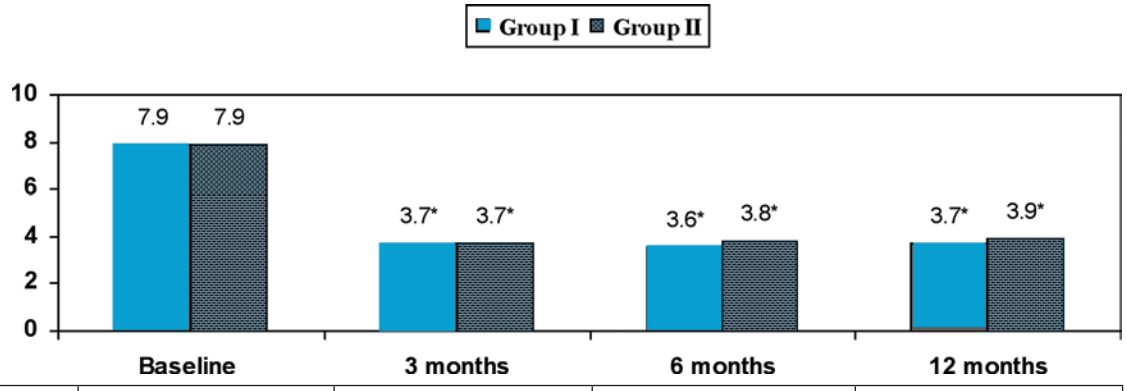


Fig. 1. *Flow diagram of selection process of literature.*

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

		Group 1 (n=36)	Group II (n=36)	P value
Gender	Male	33% (12)	47% (17)	0.337
	Female	67% (24)	53% (19)	
Age	Mean ± SD	48.7 ± 15.80	43.2 ± 13.34	0.117
Weight	Mean ± SD	195 ± 61.71	188 ± 41.3	0.577
Height	Mean ± SD	66 ± 3.95	67 ± 3.90	0.355
Duration of Pain	Mean ± SD	94 ± 68.87	108 ± 99.38	0.486
Onset of the Pain	Gradual	69% (25)	67% (24)	1.000
	Injury	31% (11)	33% (12)	
Low Back Pain Distribution	Bilateral	81% (29)	83% (30)	1.000
	Left or right	19% (7)	17% (6)	
Numeric Pain Rating Score	Mean ± SD	7.9 ± 0.82	7.9 ± 1.05	0.901
Oswestry Disability Index	Mean ± SD	26.9 ± 5.15	27.9 ± 4.96	0.417



	Baseline	3 months	6 months	12 months
Group I (n=36)	7.9 ± 0.82	3.7* ± 1.19	3.6* ± 1.13	3.7* ± 1.21
Group II (n=36)	7.9 ± 1.05	3.7* ± 1.39	3.8* ± 1.31	3.9* ± 1.55
P value	0.901	1.000	0.388	0.673

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

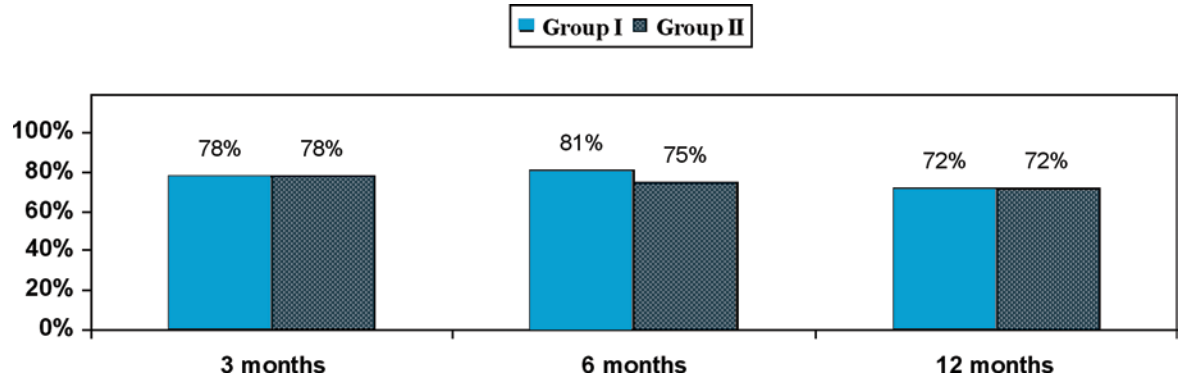
Fig. 2. *Illustration of pain relief characteristics (mean ± SD).*

Outcomes

Pain Relief

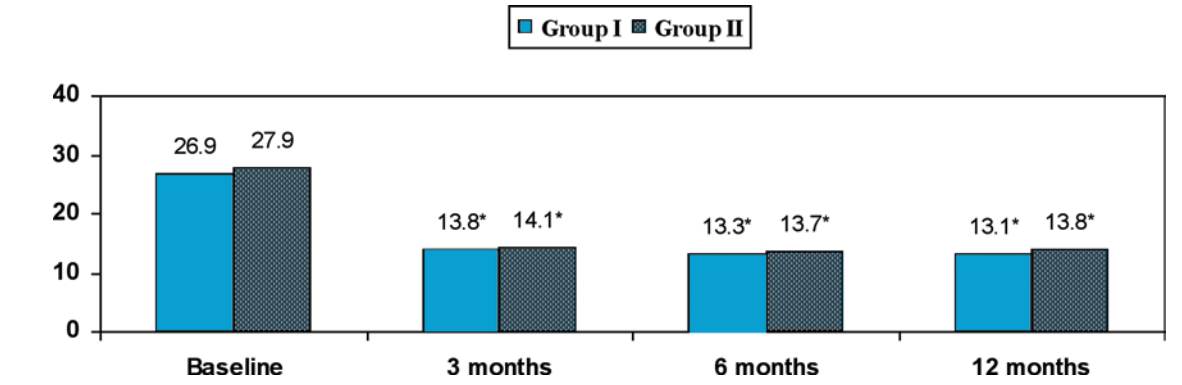
Figure 2 illustrates the NRS scores. Pain scores changed significantly from baseline, at 3 months, 6 months, and 12 months in both groups, with no significant differences between the groups or follow-up periods.

The proportion of patients with significant pain relief of 50% or greater are illustrated in Fig. 3 with 72% in both groups at 12 months. There were no significant differences between the groups or from the 3-month to 6-month to 12-month outcomes.



Group I (n=36)	78% (28)	81% (29)	72% (26)
Group II (n=36)	78% (28)	75% (27)	72% (26)
P value	1.000	0.778	1.000

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



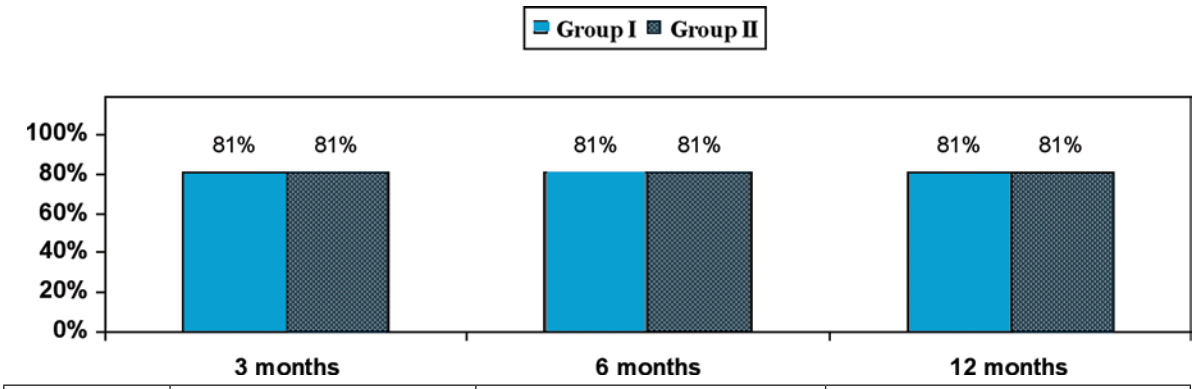
Group I (n=36)	26.9 ± 5.15	13.8* ± 4.82	13.3* ± 5.20	13.1* ± 4.86
Group II (n=36)	27.9 ± 4.96	14.1* ± 5.44	13.7* ± 5.31	13.8* ± 5.26
P value	0.417	0.837	0.721	0.532

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

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

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 81% of the patients at 3 months, 6 months, and 12 months in both groups, of the patients as shown in Fig. 5 with no significant differences noted between the groups or during follow-up periods.



Group I (n=36)	81% (29)	81% (29)	81% (29)
Group II (n=36)	81% (29)	81% (29)	81% (29)
P value	1.000	1.000	1.000

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	0	2	3
Employed full-time	5	9	6	8
Unemployed/laid off/sick	6	2	6	2
Total Employed	5	9	8	11
Eligible for employment	**11**	**11**	**14**	**13**
Housewife with no desire to work outside	4	4	3	3
Disabled	17	17	18	19
Over 65 year of age	4	4	1	1
Total Number of Patients	**36**	**36**	**36**	**36**

Employment Characteristics

Table 2 demonstrates employment characteristics in both groups. At baseline, there were 11 patients eligible for employment in Group I and 14 patients eligible in Group II, whereas the number of patients eligible for employment remained the same at 12 months in Group I and reduced to 13 in Group II. Of these, there were 5 patients employed in Group I and 8 in Group II which increased to 9 of 11 employable in Group I and 11 of 13 employable in Group II.

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 12 months.

Therapeutic Procedural Characteristics

Therapeutic procedural characteristics with average pain relief per procedure are illustrated in Table

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

Opioid intake	Group I (n=36)	Group II (n=36)	P value between groups
	Mean ± SD	Mean ± SD	
Baseline	41.4 ±38.08	46.4 ± 23.84	0.504
3 months	31.2# ± 29.93	34.7# ± 22.79	0.575
6 months	30.9# ± 30.08	38.5 ± 38.10	0.354
12 months	30.9# ± 30.08	35.3# ± 22.57	0.486

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

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=25)	Group II (n=25)	Group I (n=11)	Group II (n=11)	Group I (n=36)	Group II (n=36)
1st injection relief	7.1 ± 7.40 (25)	6.2 ± 3.50 (25)	2.6# ± 2.11 (11)	0.7 ± 1.56 (11)	5.7 ± 6.56 (36)	4.6 ± 3.96 (36)
2nd injection relief	12.6# ± 5.76 (25)	9.1 ± 3.63 (25)	0.9 ± 0.99 (10)	1.5 ± 1.41 (8)	9.3 ± 7.2 (35)	7.2 ± 4.6 (33)
3rd injection relief	12.6 ± 5.19 (22)	11.1 ± 3.22 (23)	4.6 ± 3.96 (8)	6.2 ± 4.67 (6)	10.5 ± 6.01 (30)	10.1 ± 4.02 (29)
4th injection relief	13.0 ± 4.14 (16)	12.1 ± 1.80 (21)	7.6 ± 6.11 (5)	4.4 ± 5.18 (5)	11.7 ± 5.09 (21)	10.6 ± 4.04 (26)
5th injection relief	12.1 ± 1.46 (7)	10.4 ± 4.19 (12)	13.0 (1)	12.0 ± 1.41 (2)	12.3 ± 1.39 (8)	10.6 ± 3.91 (14)
Number of injections per year	3.8 ± 0.96 (25)	4.2 ± 0.92 (25)	3.2 ± 1.17 (11)	3.0 ± 1.73 (11)	3.6 ± 1.05 (36)	3.9 ± 1.33 (36)
Total relief per year (weeks)	41.5 ± 8.48 (25)	40.4 ± 10.24 (25)	11.4 ± 11.8 (11)	8.6 ± 10.35 (11)	32.3 ± 16.93 (36)	30.7 ± 17.94 (36)

# indicates significant difference between groups ($P < 0.05$)

4. Average overall relief per year was 32.3 ± 16.93 weeks in Group I and 30.7 ± 17.94 weeks in Group II with no significant differences. However, when patients were separated into successful and failed groups, the total number of injections per year was 3.8 ± 0.96 in Group I and 4.2 ± 0.92 in Group II for successful subjects with relief of 41.5 ± 8.48 weeks in Group I and 40.4 ± 10.24 weeks in Group II. In contrast, in failed subjects the number of injections per year was 3.2 ± 1.17 in Group I and 3.0 ± 1.73 in Group II with average relief of 11.4 ± 11.8 weeks in Group I and 8.6 ± 10.35 weeks in Group II.

Epidurals were considered to be successful if a patient obtained consistent relief with the first and second injections of at least one and 3 weeks and the relief with the second injection outlasting the first injection. All others were considered as failures.

Changes in Weight

There were no significant differences in change (gain or loss) in body weight from baseline in both groups (Table 5).

Adverse Events

There were no major adverse events reported over a period of one year in 72 patients.

Table 5. *Characteristic weight monitoring.*

Weight (lbs)	Group I (n=36)	Group II (n=36)	P value
	Mean ± SD	Mean ± SD	
Initial weight	194.8 ± 61.71	187.8 ± 41.34	0.577
Weight at one year	191.6 ± 59.98	186.3 ± 42.81	0.669
Change	-3.2 ± 9.92	-1.5 ± 9.99	0.480
Participants with weight loss	53% (19)	53% (19)	0.753
Participants without change	17% (6)	11% (4)	
Participants with weight gain	30% (11)	36% (13)	

Discussion

Preliminary results of this study of 72 patients showed significant pain relief (≥ 50%) in 72% of the patients with no significant differences noted with or without steroid over a period of one-year. In addition, functional assessment measured by ODI also showed significant improvement with at least a 40% reduction in Oswestry scores in 81% of the patients with no significant differences between the groups. The average procedures per year were 3.6 ± 1.05 in Group I and 3.9 ± 1.33 in Group II with an average total relief per year of 32.3 ± 16.93 weeks in Group I and 30.7 ± 17.94 weeks in Group II over a period of 52 weeks. Further, when patients were separated into successful and failed groups, the total relief per year was 41.5 ± 8.48 in Group I and 40.4 ± 10.24 weeks in Group II among successful subjects with very low response in failed subjects. This study provides modest results with an average relief of 6 to 12 weeks with the first and second procedures in the successful group, with an average relief of 10 to 13 weeks with subsequent procedures.

The results of this study illustrate that if the response is fair to poor with the first 2 injections, they will continue to exhibit poor response with future treatments. The opioid intake was also reduced in both groups at one-year follow-up. While the results of employment are not significant, the pain relief and improvement in functional status are significant. Strict criteria were incorporated into the study and the patients only judged not to have facet joint pain were included in the study, thus avoiding the criticism of including patients with facet joint pain in the study contributing to the negative results.

There is significant controversy with regards to medical necessity and indications of lumbar epidural injections either by interlaminar approach or caudal approach. 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. The evidence for other indications is limited. Two prospective evaluations (32,33) have shown positive results in patients without disc herniation or radiculitis, but with chronic function-limiting low back pain. In these studies, patients without facet joint pain were evaluated under fluoroscopy. As illustrated in the present study, epidural injections do not provide long-term relief. However, long-term relief can be achieved with judicious use and appropriate evaluation in patients without facet joint pain, lasting on average, 10 to 13 weeks in the phase after 2 initial injections. These results are similar to the patients receiving caudal epidural injections either with or without steroids with disc herniation and radiculitis (45), but superior to patients suffering with spinal stenosis and post-surgery syndrome (46,47). Finally, the results of this randomized, equivalence trial reinforce and validate the previous findings in prospective evaluations.

The results of this evaluation are generalizable to interventional pain management settings with appropriate diagnostic techniques and under fluoroscopic visualization. Since this is an equivalence trial, it is also considered a practical clinical trial. The results of this study are applicable to individual patients or groups that differ from those controlled in the placebo trials. In the era of evidence-based medicine, pragmatic or practical clinical trials measuring effectiveness are considered more appropriate than explanatory trials measuring efficacy (37,48-52). Explanatory trials measure efficacy, whereas pragmatic or practical trials are best designed to provide the results of benefit of the treatment produced in routine clinical practice. In ad-

dition, in this study the evidence is based on head-to-head comparisons of clinically relevant alternatives — namely local anesthetic with or without steroids. A placebo-controlled trial measures absolute effect size and shows existence of effect. In contrast, an active control trial such as the present study not only shows the existence of effect, but also compares therapies (53).

The study may be criticized for the lack of placebo group and preliminary analysis. However, considering the difficulties related to placebo groups in interventional techniques in the United States, the present study with local anesthetics with or without steroid is appropriate. Further, even though it is a preliminary analysis, the number of patients included in this analysis exceeds the sample size calculation of 58 subjects.

The issue of 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, thus, this provides internal validity. This study may resolve to some extent the issue of the local anesthetics with or without steroids in managing chronic function-limiting low back pain without disc herniation, radiculitis, or facet joint pain. These results describe patients in a private practice, interventional pain management setting in a practical and pragmatic clinical trial. Consequently, the results are not applicable in the general population unless the same methodology is utilized with the diagnosis and therapy. Further, generalizability of the findings of this study may only be feasible in studies utilizing larger populations in multiple settings.

The underlying mechanism of action of epidurally administered steroid and local anesthetic injection is still 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 (13,54,55). Further, 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 (54-63). In contrast, local anesthetics have been described to provide short- to long-term symptomatic relief based on various mechanisms (64-76). It has been described that multiple pathophysiologic mechanisms may be involved in chronic pain including noxious peripheral stimulation, excess nociceptive process resulting in the sensitization of the pain pathways at several neuronal levels (64,65), and excess release of neurotransmitters causing complex central responses including hyperalgesia or wind-up (63), resulting in an increase in nociceptive sensitization of the nervous system (66,67), and phenotype changes which are also considered as part of the neuronal plasticity (66-68). Consequently, it has been postulated that local anesthetics may provide analgesia by suppression of nociceptive discharge, the block of axonal transport (74,75), the block of the sympathetic reflex arc (67,73), the block of sensitization (64,65), anti-inflammatory effect (76), and blockade of axonal transport of nerve fibers at lower concentrations compared with those that are necessary for a block of a nerve conduction (74,75). The long-lasting effect of local anesthetics in epidural injections has been demonstrated in a multitude of studies (32,33,39-41,73,75-85). Sato et al (84) evaluated the prolonged analgesic effect of epidural bupivacaine in a rat model of neuropathic pain and concluded that repetitive administration of bupivacaine into the epidural space in rats exerts an analgesic effect, possibly by inducing a plastic change in nociceptive input. Further, Tachihara et al (85) 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.

Multiple studies have reported that not only mechanical compression due to intervertebral disc protrusion, but also nociceptive and inflammatory mediators originating from the nucleus pulposus, play important roles in the onset of pain in lumbar disc herniation (85-97). Corticosteroids have therapeutic effects on radicular symptoms caused by lumbar disc herniation due to their anti-inflammatory function. Furthermore, corticosteroids reportedly ameliorate early vascular permeability increases in spinal nerve roots and inhibit reductions in nerve conduction velocity induced by epidural application of nucleus pulposus (56). Finally, corticosteroids may exert "anesthetic like" actions on nociceptive C fiber conduction independent of anti-inflammatory properties (98). However, corticosteroids are also known to possess direct neurotoxic effects on peripheral nerve tissue (55,62,99,100) unlike local anesthetics.

Overall, the evidence in this report demonstrates caudal epidural injections in patients negative for lumbar facet joint pain confirmed by controlled, comparative local anesthetic blocks with a criteria of 80%

pain relief, which is not sustainable after prior painful movements for appropriate duration of action of local anesthetic, without disc herniation or radiculitis, may be treated with caudal epidural injections with or without steroids, providing approximately 12 weeks of relief with each procedure and requiring 3–4 episodes of treatment per year.

Conclusion

The assessment of the preliminary results of this randomized, controlled, equivalence trial of caudal epidural injections in chronic function-limiting low back pain without facet joint pain, disc herniation, and/or radiculitis demonstrated effectiveness in over 70% of the patients with improvement in functional status.

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