Randomized Trial

Effect of Fluoroscopically Guided Caudal Epidural Steroid or Local Anesthetic Injections in the Treatment of Lumbar Disc Herniation and Radiculitis: A Randomized, Controlled, Double Blind Trial with a Two-Year Follow-Up

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Background: Lumbar disc herniation and radiculitis are common elements of low back and lower extremity pain. Among minimally invasive treatments, epidural injections are one of the most commonly performed interventions. However, the literature is mixed about their effectiveness in managing low back and lower extremity pain. In general, individual studies and systematic reviews of epidural steroid injections have been hampered by their study design, baseline differences between treatment groups, inadequate sample sizes, highly controlled settings, lack of validated outcome measures, and the inability to confirm the injectate location because fluoroscopy was not used.

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

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

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

Methods: One hundred twenty patients were randomized to two groups: Group I received 10 mL caudal epidural injections of local anesthetic, lidocaine 0.5%; Group II patients received caudal epidural injections of 0.5% lidocaine, 9 mL, mixed with 1 mL of steroid.

Outcome Assessment: Multiple outcome measures were utilized. The primary outcome measures were Numeric Rating Scale (NRS) and the Oswestry Disability Index 2.0 (ODI). Secondary outcome measures were employment status and opioid intake.

Significant pain relief improvement was defined as 50% or more improvement in NRS and ODI scores.

Results: In the successful category, 77% of Group I had significant pain relief of ≥ 50% and functional status improvement of ≥ 50% reduction in ODI scores; in Group II it was 76%, whereas overall it was 60% and 65% in Groups I and II. Over the two years, Group I had an average number of procedures of 5.5 ± 2.8; Group II was 5.3 ± 2.4. Even though there was no significant difference in overall relief between the two groups, the average relief for each procedure was superior for steroids.

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

Conclusion: Caudal epidural injections of local anesthetic with or without steroids might be an effective therapy for patients with disc herniation or radiculitis. The present evidence illustrates the potential superiority of steroids compared with local anesthetic at two year follow up based on average relief per procedure.

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

Trial Registration: NCT00370799

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Over the past 77 years, voluminous literature has been written describing the epidemiology, diagnosis, and numerous treatment modalities for herniated disc pain, following the description of disc herniation by Mixter and Barr in 1934 (1-26). The estimated prevalence of lumbar radiculopathy or sciatica has been described as 9.8 per 1,000 cases (4), 5.1% in men and 3.7% in women (3). However, lumbar radiculopathy secondary to disc herniation resolves spontaneously in 23% to 48% of patients, but up to 30% to 70% will still have pronounced symptoms after one year, with 5% to 15% of patients undergoing surgery resulting in high economic impact and strain on health services (6,7,16,24-26). Among minimally invasive treatments, epidural injections are one of the most commonly performed interventions (2,17-21,24-33). However, the literature is mixed about their effectiveness in managing low back and lower extremity pain (2,17,20,21,24-32). In general, individual studies and systematic reviews of epidural steroid injections have been hampered by their study design, baseline differences between treatment groups, inadequate sample sizes, highly controlled settings, lack of validated outcome measures, and the inability to confirm the injectate location because fluoroscopy was not used (2,17,20,21,25-38). Other problems include inappropriate methodology, improper study evaluation, and evidence synthesis for systematic reviews (2,17,21,25,26,31-33). Further, the three different approaches, caudal, interlaminar, and transforaminal, are used to treat multiple pathologies including disc herniation, axial or discogenic pain, spinal stenosis, and lumbar postsurgery syndrome along with other causes of low back pain. Thus, combining patients and/or results yielded significant confusion. Incorrect needle placement has been demonstrated in 20% to 38% of patients who have caudal epidural injections without fluoroscopy (34-38). Consequently, most systematic reviews (2,20,21,25,26,31-33) have included non-fluoroscopically guided studies; some recent studies also were published without fluoroscopy (27,29). Recently, Manchikanti et al (30) published the results of fluoroscopic caudal epidural injections in the treatment of lumbar disc herniation and radiculitis in a randomized, controlled, double blind trial and showed the proportion of patients with significant pain relief of 50% or greater and/or improvement in functional status with 50% or more reduction in ODI scores to be 70% and 67% in patients receiving local anesthetic only, and 77% and 75% in patients receiving steroids with average procedures per year of 3.8. In contrast, Iversen et al (27) in a recent multicenter, blinded, randomized control trial evaluating the effect of caudal epidural steroid or saline injection for chronic lumbar radiculopathy without fluoroscopy, at 52 weeks showed no significant difference among placebo injection of 2 mL of sodium chloride solution over the sacral hiatus, 40 mL injection of sodium chloride solution into the epidural space, or 40 mg of triamcinolone mixed with 40 mL of sodium chloride solution.

The multiple differences between these studies can be attributed to Iversen et al (27) using ultrasound, a technique which has not been proven to identify the caudal epidural space accurately. On the other hand, Manchikanti et al (30) used fluoroscopy. There were also multiple flaws with the design, conduct, and interpretation of the results with probable inclusion of acute pain patients, inappropriate conservative management since a significant proportion of patients improved prior to their randomization or starting treatment, using large volumes that diluted the steroid, and the lack of use of local anesthetic (27,39,40). Further, approximately 40% of the patients were excluded with neurologic problems that did not fit the inclusion criteria, including a large proportion of patients with arachnoiditis, a rare condition (27).

In contrast, Manchikanti et al (30) conducted the study in a truly chronic population who had disc herniation and radiculitis for at least six months and who had failed conservative management. In this study fluoroscopy was used and injections were performed based on the return of pain and deterioration in functional status.

Thus, there continues to be conflicting evidence regarding the benefit of epidural steroid injections with or without local anesthetic. Thus far, only three randomized, controlled trials have been published evaluating mid term or long term outcomes with fluoroscopically guided caudal epidural injections (28,30,41). Ackerman and Ahmed (41) only reported outcomes at 24 weeks in 30 patients. Dashfield et al (28) utilized only one injection when comparing endoscopic delivery of steroids in 27 patients and only six months of follow up. Even so, they reported positive results. The results of Manchikanti et al (30) with one year followup were positive in a practical, clinical setting.

This study was undertaken to evaluate the role of caudal epidural injections in patients with chronic low back and lower extremity pain secondary to disc herniation and radiculitis. This report is a continuation

of the results of a previous publication (30) reflecting the results of the comparative effectiveness of caudal epidural injections of local anesthetic with or without steroids. This report contains data from the long term followup of two years.

Methods

This randomized, double blind, controlled trial was conducted based on the Consolidated Standards of Reporting Trials (CONSORT) (42). The study was approved by the Institutional Review Board (IRB) and was registered with the U.S. Clinical Trial Registry. It was conducted in an interventional pain management practice in the United States. Patients were recruited from new patients presenting to a single pain management center.

Interventions

All patients were provided with the approved protocol and informed consent that described the study and withdrawal process.

Patients were assigned into two groups. Group I patients received caudal epidural injections under fluoroscopy of local anesthetic (lidocaine 0.5%), while Group II patients received caudal epidural injections of lidocaine mixed with steroids.

Pre-Enrollment Evaluation

The preenrollment evaluation consisted of specific data and outcome parameters. Outcome parameters included numeric rating scale (NRS), Oswestry Disability Index 2.0 (ODI), work status, and opioid intake. Demographic data included medical and surgical history with coexisting disease(s), radiologic investigations, and physical examination findings.

Inclusion Criteria

For patients to be included in the study, essential requirements were demonstrated disc herniation with radiculitis; age over 18 years; function limiting low back and lower extremity pain of at least six months; and, finally, patients who were competent and willing to participate in the study protocol and who could provide voluntary, written informed consent.

Exclusion criteria were: patients with a previous history of lumbar surgery; radiculitis secondary to either central or foraminal stenosis; no disc herniation; uncontrollable or unstable opioid use; uncontrollable psychiatric disorders; uncontrolled medical illness, either acute or chronic; pregnant or lactating women; a history or potential for adverse reactions from local anesthetic or steroid; and any conditions that could interfere with the interpretation of the outcome measurements.

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 an #18 gauge Tuohy needle, with the patient in the prone position. Appropriate monitoring with intravenous access and sedation with midazolam and fentanyl were provided as needed. Access to the epidural space was confirmed by injection of non-ionic contrast medium, followed by injection of 10 mL of lidocaine hydrochloride 0.5% preservative free into 60 Group I patients, and in Group II 9 mL of lidocaine mixed with 6 mg of betamethasone (either brand name or non-particulate) or 40 mg of methylprednisolone was injected. Twenty patients in Group II each received one of the three steroids.

Additional Interventions

Additional or repeat caudal epidural injections were provided on the basis of the patient's response, either after unblinding or without unblinding. All unblinded patients were considered to be withdrawn from the study. Non-responsive patients who did not receive further interventions were followed without unblinding.

Cointerventions

There were no specific cointerventions or additional interventions. However, all patients continued previous exercise programs, drug therapy, and work.

Objectives

The design of the study was a randomized, double blind, active control 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.

Outcomes

The primary outcomes were pain relief and functional status improvement based on NRS pain scales and ODI disability scale. The secondary outcomes were employment and opioid intake.

The NRS pain scale (0-10), the ODI disability scale on a 0 to 50 scale, employment status, and opioid intake in terms of morphine equivalents were assessed at 3, 6, 12, 18, and 24 months posttreatment. The reliability of the NRS and ODI have been reported (43,44).

Significant pain relief and functional improvement of 50% or more reduction in NRS or ODI from baseline have been deemed appropriate (45-50).

The opioid intake was converted into morphine equivalents on the basis of the dosage frequency and schedule of the drug (51).

Employment and work status were classified into multiple categories based on present employment, unemployment due to pain, housewife with no desire to work outside the home, retirement, or over the age of 65 years. Patients who were unemployed because of pain or employed but on sick leave or laid off were considered as employable.

Patient response was considered successful if a patient obtained consistent relief lasting at least a total of three weeks with the first two procedures. Patients with less than three weeks of relief were considered as failures.

Sample Size

Sample size was calculated on the basis of significant pain relief and improvement in functional status. Considering a 0.05 two sided significance level, a power of 80%, and an allocation ratio of 1:1, 55 patients in each group were estimated (52). Allowing for a 10% attrition/non-compliance rate, 60 patients were required.

A previous Cochrane systematic review of epidural injections (33), and multiple other studies (45-50) identified 50 to 60 patients as acceptable; others have identified even smaller samples (27,53).

Randomization

Sixty patients were randomly assigned into each group, for a total of 120 patients.

Sequence Generation

A computer generated random allocations sequence by simple randomization was used for randomization.

Allocation Concealment

Based on randomization, drugs were prepared by the operating room nurse assisting with the procedure.

Implementation

Patients meeting inclusion criteria were invited to enroll in the study. One of the three nurse coordinators of the study enrolled the participants and assigned participants to their

Blinding (Masking)

Participants, those administering the interventions, and all others involved in patient care were blinded to the group assignments. The blinding was also 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 or their group assignment.

Statistical Methods

Data analyses were carried out using the Statistical Package for Social Sciences version 9.01 (SPSS Inc, Chicago, IL). For categorical and continuous data comparison, Chi-square (Fisher test where necessary) and t test were used respectively. Because the outcome measures of the participants were measured at 4 points in time, repeated measures analysis of variance were performed with the post hoc analysis. A P value of less than 0.05 was considered significant.

There were no significant differences noted among the three subgroups receiving steroids in any outcome parameters or the frequency of interventions. Thus, the three subgroups receiving steroids were considered as one group (group II).

Intent-to-Treat Analysis

An intent-to-treat analysis was performed. A sensitivity analysis with changes in the NRS was performed utilizing the last follow-up score, best case scenario, and worst case scenario if there were no significant differences; the intent-to-treat analysis with last follow-up visit was used.

Results

Patient Flow

Figure 1 illustrates the participant flow.

Recruitment

The recruitment period started in January 2007 and ended in October 2009.

Baseline Characteristics

Table 1 illustrates the baseline demographic and clinical characteristics of each group.

There were differences in the demographic characteristics with respect to age, weight, and mode of pain onset.

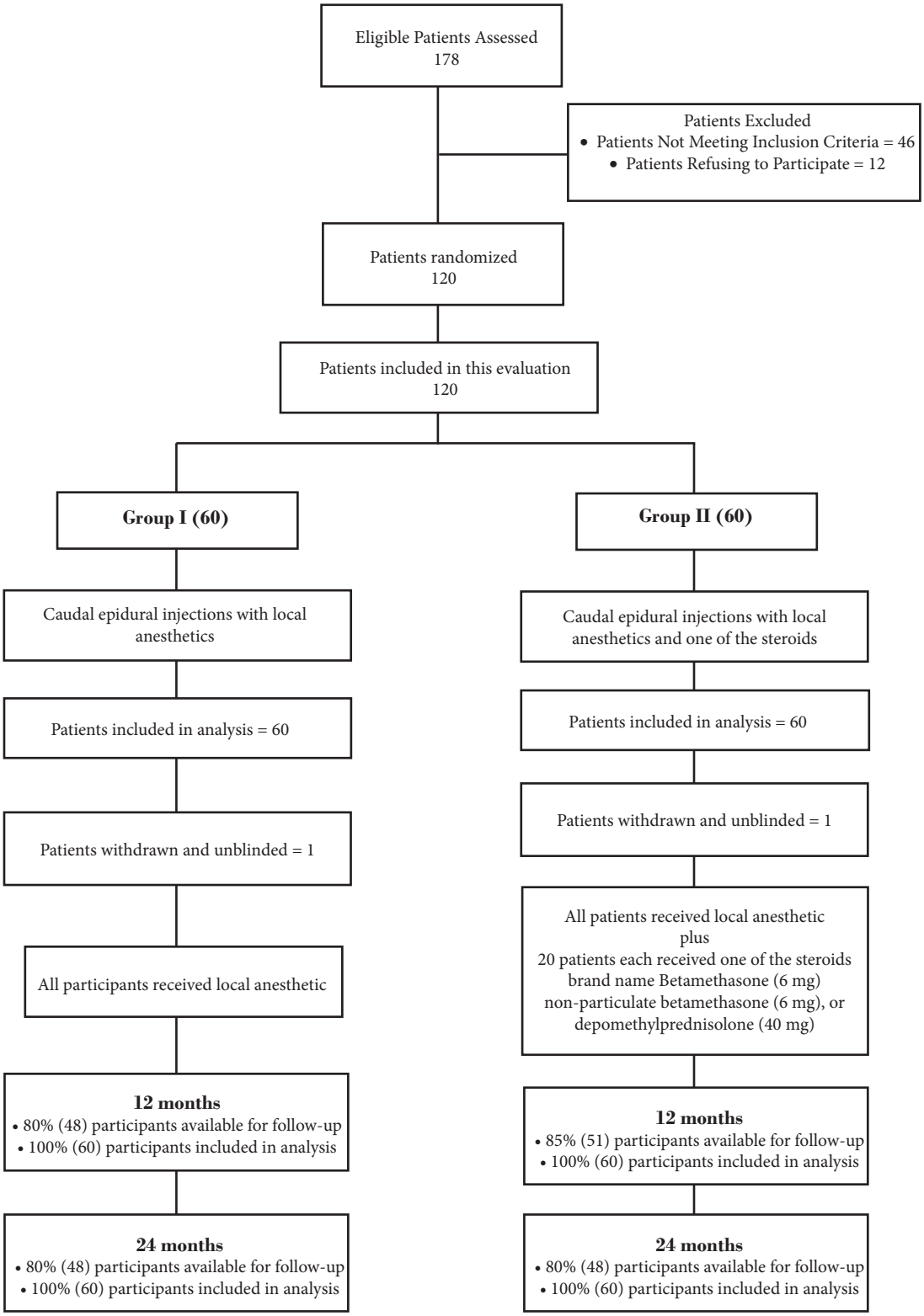

Fig. 1. *Schematic presentation of patient flow at 2 year follow-up of 60 patients.*

Table 1. *Baseline demographic characteristics*.

		Group 1 (60)	Group II (60)	P value
Sex	Male	32% (19)	38% (23)	0.566
	Female	68% (41)	62% (37)	
Age	Mean ± SD	48.7 ± 14.1	43.0 ± 14.5	0.031
Weight	Mean ± SD	208.3 ± 53.9	177.5 ± 46.8	0.001
Height	Mean ± SD	66.2 ± 3.5	66.6 ± 4.0	0.580
Duration of Pain (Months)	Mean ± SD	93.4 ± 86.9	81.3 ± 81.7	0.436
Onset of Pain	Gradual	72% (43)	52% (31)	0.034
	Injury	28% (17)	48% (29)	
Numeric Rating Score	Mean ± SD	8.1 ± 0.9	7.8 ± 0.9	0.077
Oswestry Disability Index	Mean ± SD	29.2 ± 4.6	27.9 ± 4.8	0.158
Disc Herniation * (levels)	L3/4	8% (5)	5% (3)	NS
	L4/5	67% (40)	70% (42)	
	L5/S1	58% (35)	50% (30)	

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

Analysis of Outcomes

Pain Relief & Functional Assessment

Table 2 presents the results of repeated measures analysis. There were significant differences in participants' average pain scores within group by time ($P < 0.0001$), and no significant differences between two groups ($P = 0.802$). In the Oswestry Disability Index for functional status, there were significant differences in summary scores within group by time ($P = 0.001$) and no significant differences between two groups ($P = 0.705$). Paired samples t-test analysis indicates that mean differences baseline and the other five time points within the group were significant at the 0.05 level.

Employment Characteristics

Table 3 illustrates employment characteristics.

Opioid Intake

Table 4 illustrates opioid intake converted to morphine equivalents.

Therapeutic Procedural Characteristics

Therapeutic procedural characteristics and average pain relief data are illustrated in Table 5. The relief attained was significantly higher in Group II, the group that received steroids, compared with Group I for the first two procedures; the average relief per procedure over two years was also higher in Group II. When patients were separated into successful and failed groups, the total number of injections per year was 4.3 ± 1.0 and 6.5 ± 2.4 for two years in Group I and 3.8 ± 1.0 per year and 5.8 ± 2.2 for two years in Group II in the successful group. Total relief was 70.1 ± 30.8 weeks in Group I and 76.5 ± 27.7 weeks in Group II for two years in successful category.

Figure 2 illustrates outcome data percentages of all participants, failed participants, and successful participants.

Changes in Weight

There were no differences in change (gain or loss) in body weight from baseline within the groups (Table 6).

Adverse Events

There were no major adverse events reported over a period of two years in all 120 patients.

Table 2. *Comparison of Numeric Rating Scale for pain and Oswestry Disability Index score summaries at 4 time points.*

Time Points	Numeric Pain Rating scale		Oswestry Disability Index	
	Group I (60)	Group II (60)	Group I (60)	Group II (60)
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
Baseline	8.1 ± 0.9	7.8 ± 0.9	29.2 ± 4.6	27.9 ± 4.8
3 months	4.1* ± 1.8 (77%)	3.4* ± 1.7 (80%)	16.5* ± 7.2 (62%)	13.6* ± 6.5 (73%)
6 months	3.9* ± 1.8 (77%)	3.5* ± 1.7 (82%)	15.5* ± 7.3 (72%)	13.7* ± 7.0 (73%)
12 months	4.1* ± 1.8 (70%)	3.5* ± 1.9 (77%)	15.5* ± 7.74 (67%)	13.1* ± 7.0 (75%)
18 months	4.1* ± 1.8 (65%)	3.5* ± 1.8 (75%)	15.5* ± 7.4 (62%)	13.2* ± 6.7 (77%)
24 months	4.2* ± 1.8 (63%)	3.6* ± 1.8 (68%)	15.6* ± 7.3 (60%)	13.5* ± 7.2 (70%)
Group Difference	0.802		0.705	
Time Difference	0.001		0.001	
Group by Time Interaction	0.036		0.053	

Lower the value indicates better condition
* significant difference with baseline values within the group ($P < 0.05$)
(____) illustrates proportion with significant pain relief (≥ 50%) from baseline

Table 3. *Employment characteristics.*

Employment status	Group I			Group II		
	Baseline	12 Months	24 Months	Baseline	12 Months	24 Months
Employed Part-time	2	3	3	7	6	5
Employed Full-time	9	13	13	8	20	20
Unemployed	5	1	1	11	1	1
Total Employed	11	17	17	15	26	25
Eligible for Employment	16	16	16	26	26	26
Housewife	5	4	3	5	4	4
Disabled	31	31	32	23	23	24
Over 65 Years Old	8	8	8	6	6	6
Total Number of Patients	60	60	60	60	60	60

Discussion

This randomized, active control trial of 120 patients with chronic persistent low back and lower extremity pain secondary to disc herniation and radiculitis, assessing caudal epidural injections with or without steroids, showed clinically meaningful and significant improvement in all parameters at the end of a two year period. The results of this study illustrate that in carefully selected patients, judged as successful participants who responded to the first two initial procedures, combined pain relief and improvement in functional status was observed in 77% in Group I and 76% in Group II at two year follow up. However, overall improvement was also significant with 60% of the patients showing improvement in Group I and 65% of the patients in Group II. Consequently, this study confirms the failure of the null hypothesis that treatment of chronic lumbar radiculopathy with caudal epidural injections of

Table 4. *Opioid intake (morphine equivalents in mg).*

Opioid Intake (Morphine Equivalents in mg)	Group I (60)	Group II (60)
	Mean ± SD	Mean ± SD
Baseline	51.8 ± 58.6	45.0 ± 57.8
3 Months	32.8* ± 31.6	30.1 ± 31.8
6 Months	32.9* ± 31.6	31.1 ± 37.5
12 Months	32.8* ± 31.6	31.1 ± 37.5
18 Months	32.8* ± 31.6	31.1 ± 37.5
24 Months	32.8* ± 31.6	31.1 ± 37.5
Group Difference	0.753	
Time Difference	0.004	
Group by Time Interaction	0.492	

* significant difference with baseline values (P < 0.05)

Table 5. *Therapeutic procedural characteristics with procedural frequency, average relief per procedure, and average total relief in weeks over a period of one and two years.*

	Successful Patients		Failed Patients		Overall Results	
	Group I (47)	Group II (50)	Group I (13)	Group II (10)	Group I (60)	Group II (60)
Average Number of Procedures First Year	4.3# ± 1.0	3.8 ± 1.0	2.1 ± 1.2	2.5 ± 1.2	3.8 ± 1.4	3.6 ± 1.1
Average Number of Procedures Over 2 Years	6.5 ± 2.4	5.8 ± 2.2	2.2 ± 1.1	2.6 ± 1.4	5.5 ± 2.8	5.3 ± 2.4
Average Relief per Procedure for Initial 2 Procedures in Weeks (Maximum)	6.6* ± 3.8 (17 weeks)	11.3 ± 14.6 (100 weeks)	1.4 ± 2.2 (8 weeks)	1.3 ± 2.6 (11 weeks)	5.6* ± 4.1 (17 weeks)	9.7 ± 13.9 (100 weeks)
Average Relief per Procedure After Initial 2 Procedures (Maximum)	12.7* ± 3.5 (36 weeks)	14.4 ± 9.2 (94 weeks)	4.8 ± 5.4 (13 weeks)	7.3 ± 9.4 (26 weeks)	12.5* ± 3.7 (36 weeks)	14.1 ± 9.2 (94 weeks)
Average Relief per Procedure	10.8* ± 4.7	13.3 ± 11.4	2.1 ± 3.4	2.9 ± 5.8	10.1* ± 5.0	12.5 ± 11.4
Average Total Relief First Year (Weeks)	40.7 ± 11.4	42.7 ± 11.0	4.5 ± 7.1	7.1 ± 10.4	32.9 ± 18.4	36.8 ± 17.2
Average Total Relief Over 2 Years (Weeks)	70.1 ± 30.8	76.5 ± 27.7	4.5 ± 7.0	7.5 ± 11.7	55.9 ± 38.6	65.0 ± 36.5

* significant difference Group II (P < 0.05)
Successful group - At least three weeks of relief with first 2 procedures

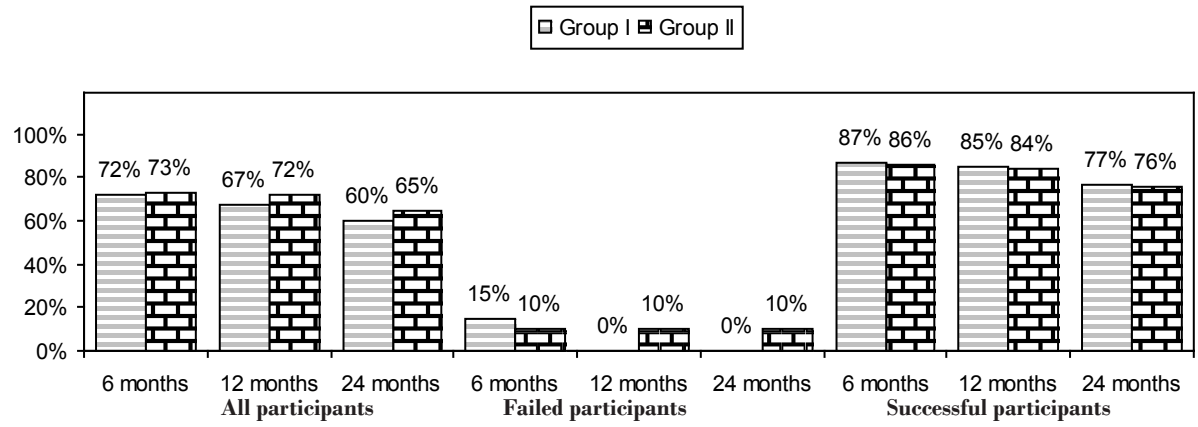

Fig. 2. *Proportion of patients with significant reduction in Numeric Rating Score and Oswestry Disability Index (≥ 50% reduction from baseline).*

Table 6. *Characteristics of weight monitoring.*

Weight (lbs)	Group I (60)	Group II (60)	P value
	Mean ± SD	Mean ± SD	
Weight at Beginning	208.3 ± 53.9	177.5 ± 46.8	0.001
Weight at One Year	202.9 ± 52.2	176.8 ± 46.8	0.009
Change	5.3 ± 10.9	0.9 ± 15.0	0.014
Lost Weight	27% (16)	37% (22)	0.495
No Change	18% (11)	15% (9)	
Gained Weight	55% (33)	48% (29)	
Weight at Two Years	202.4 ± 52.9	178.0 ± 46.8	0.009
Change	-5.9 ± 12.8	0.5 ± 9.7	0.003
Lost Weight	53% (32)	50% (30)	0.047
No Change	22% (13)	8% (5)	
Gained Weight	25% (15)	42% (25)	

steroids or local anesthetic has no clinically important effect. Instead, it confirms that the treatment of lumbar disc herniation with radiculopathy with caudal epidural injection of steroids or local anesthetics has clinically important effects, irrespective of the steroid utilized, whether it is methylprednisolone, brand name betamethasone, or non-particulate betamethasone mixed with local anesthetic. While the average total relief over two years was not significantly different—70.1 ± 30.8 weeks in Group I and 76.5 ± 27.7 weeks in Group II in the successful group— the average relief per procedure for the initial two procedures, as well as subsequent procedures and overall procedures over the period of two years, was significantly higher in Group II, not only in the successful patients, but also with reference to overall results. Thus, steroids indicate a potential superiority on a long term basis over a two year period, requiring approximately six procedures over two years, whereas it was slightly higher for Group I without steroids at 6.5 procedures for two years. We also observed a significant decrease in opioid intake from the baseline in Group I and an insignificant decrease in opioid intake in Group II along with an insignificant increase in employment in both groups at two years. At the end of two years, almost all of the patients eligible for employment in both groups were employed. We expected significant weight gains in the steroid group, however, there was no change noted in patients gaining weight at the end of one year. There was a significant proportion of patients gaining weight at the end of two years. This is significant since baseline weights were significantly higher in Group I, thus this finding may indicate that over a long-term period steroids may contribute to weight gain even though this change was absent at the end of one-year.

The literature is replete with multiple studies and systematic reviews in favor of and against epidural injections in general (2,17,20,21,25-33). Multiple studies have been criticized, most importantly for their design and their inability to confirm the location of the injectate by not using fluoroscopy. Systematic reviews have been criticized for their methodology by evaluating the studies inappropriately; consequently their evidence synthesis has led to inaccurate conclusions.

In a systematic review by Conn et al (17) of randomized trials of caudal epidural injections for managing chronic low back pain of various origins, including disc herniation, only two trials met the inclusion criteria of long term follow up of at least six months and the use of fluoroscopic visualization (28,54). They concluded that patients receiving caudal epidural injections with or without steroids had better results when the injections were performed under fluoroscopy. The authors did not include one study because of a 24 week follow up, which also showed positive results (41). Other systematic reviews (20,21,33) have combined multiple approaches into one category; the majority of them did not use fluoroscopy.

Since the publication of these systematic reviews, new studies were published (27,29,30) confirming the effectiveness of epidural injections (29,30), even without fluoroscopy in one study (29), and showing nega-

tive results in one study (27). Iversen et al (27) published a placebo controlled study under ultrasound without fluoroscopy showing negative results, however the study has been criticized for multiple flaws with design, conduct, patient selection, lack of fluoroscopy, and interpretation of the results (39,40). Further, Cohen (55) in an editorial accompanying Iversen et al (27), commented that overall epidural steroid injections seem to be beneficial, but only provide modest improvement in carefully selected patients with predominantly radicular symptoms. Cohen believed that there was no definitive answer and postulated multiple reasons for the failure of epidural steroid injections in Iversen et al's study (27). Despite the negative findings, Cohen believed that Iversen et al's study should not be misinterpreted as suggesting that epidural steroid injections are of no use in neuropathic back pain. He also commented that if only a small proportion of people return to work or can avoid surgery, epidural steroid injections may be considered as an effective adjunct when used judiciously. Thus, in the era of comparative effective research (31,32,56-58), the evidence from comparative effectiveness or active controlled trials such as the present study are crucial in selecting a clinical intervention.

In recent years, comparative effectiveness research has been considered pivotal to evidence based medicine (31,32,56-58). Even though the current study is limited to a single center, it is randomized, active controlled, and double blind, designed to determine whether fluoroscopically directed epidural injections with or without steroids with usual volumes injected in practice are helpful. Consequently, the results of this trial are applicable to interventional pain management in practical settings. Patient selection was not only practical but also was met with great sensitivity and included only patients with chronic persistent pain due to disc herniation and radiculitis. Consequently, this study meets the criteria for pragmatic or practical clinical trials with an active control group instead of a placebo group, and measures effectiveness, which is considered more appropriate than explanatory trials measuring efficacy (43,59-62). In addition, the current study was made as practical as possible by utilizing injection therapy with repeat caudal epidural injections based on the requirement that there be an increase in pain and deterioration in functional status prior to repeating the injection, rather than following a routine of a certain number of procedures, inappropriate assessment, and expecting one or two years of positive outcomes with one procedure. Further, as seen in contemporary specialized practices, this study demonstrated that the first or the initial two procedures do not provide long term relief, and if the initial relief does not last more than three weeks, the procedures may not provide relief in patients on a long term basis as was observed in failed patients, and that it may be futile to continue to repeat these procedures in these patients, unless there are compelling reasons.

Further, this study may be criticized by not focusing on clinical aspects and as deficient because of the lack of a placebo group. However, most studies have utilized inappropriate methodology of placebo groups (27,63-68). The appropriate placebo design by Ghahreman et al (67) showed no significant effect with sodium chloride solution when injected into an inactive structure. Further, these concepts, including local anesthetic transformed into placebo, are not only methodologically and conceptually inaccurate, they also result in misleading conclusions since inactive substances injected into active structures have been shown to result in various types of effects (69-72) and local anesthetics have been shown to provide long term improvement in patients both in clinical as well as experimental settings (45-50,73-85).

Further, an Institute of Medicine (IOM) report states that the effectiveness of pain treatments depends greatly on the strength of the clinician-patient relationship: Pain treatment is never about the clinician's intervention alone, but about the clinician and the patient (and family) working together (86).

Finally, other weaknesses include differences in baseline demographic characteristics with respect to weight, age, and the pain's mode of onset. However, these differences may be considered minor and have not shown to have any effect on the final results.

Even though the mechanism of action of steroids and local anesthetics continues to be debated and multiple hypothesis are emerging, the evidence shows that steroids as well as local anesthetics have significant effects on the modulation of noxious stimulation by various mechanisms (73-78,87-90) with no significant difference whether local anesthetics are injected alone or with steroids (45-50,79-85).

Implications of this trial are enormous in an era of evidence based medicine, comparative effectiveness research, and exploding health care costs. Studies with proper methodology in practical settings are crucial. Proper application of the interventions will improve patient's pain function, reduce drug use, and may return them to the work force – a great benefit for society.

However, inappropriate provision of any type of intervention, specifically one which incurs substantial expenses, will not provide any benefit, harm the patient, and deplete resources, thus reducing access. Similarly, inappropriately performed evaluations that lead to inaccurate conclusions may reduce health care expenditures, but will also increase patient suffering, reduce function, increase drug use, and finally impede access to medical care.

Conclusion

This randomized double blind, active controlled trial of 120 patients treated with fluoroscopically guided caudal epidural injections of local anesthetic with or without steroids for chronic low back and lower extremity pain secondary to disc herniation and radiculitis, illustrated effectiveness in more than 75% of the patients with improvement in functional status, requiring an average of six procedures over two years and providing over 70 weeks of pain relief and function status improvement during the two year period in appropriately selected patients.

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