

Research Article

Lumbar Interlaminar Epidural Injections Are Superior to Caudal Epidural Injections in Managing Lumbar Central Spinal Stenosis

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Background: Epidural injections are performed to manage lumbar central spinal stenosis pain utilizing caudal, interlaminar, and transforaminal approaches. The literature on the efficacy of epidural injections in managing lumbar central spinal stenosis pain is sparse; lacking multiple, high quality randomized trials with long-term follow-up.

Methods: Two randomized controlled trials of the caudal and lumbar interlaminar approaches that assessed 220 patients with lumbar central spinal stenosis were analyzed.

Results: The analysis found efficacy for both caudal and interlaminar approaches in managing chronic pain and disability from central spinal stenosis was demonstrated. In the patients responsive to treatment, those with at least 3 weeks of improvement with the first 2 procedures, 51% reported significant improvement with caudal epidural injections, whereas it was 84% with local anesthetic only with interlaminar epidurals, 57% with caudal and 83% with lumbar interlaminar with local anesthetic with steroid. The response rate was 38% with caudal and 72% with lumbar interlaminar with local anesthetic only and 44% with caudal and 73% with lumbar interlaminar with local anesthetic with steroid when all patients were considered. In the interlaminar approach, results were superior for pain relief and functional status with fewer nonresponsive patients compared to the caudal approach.

Limitations: The data was derived from 2 previously published randomized, controlled trials rather than comparing 2 techniques in one randomized controlled trial. Further, the randomized controlled trials were active control trials without a placebo.

Conclusions: The results of this assessment showed significant improvement in patients suffering with chronic lumbar spinal stenosis with caudal and interlaminar epidural approaches with local anesthetic only, or with steroids in a long-term follow-up of up to 2 years, in contemporary interventional pain management setting, with the interlaminar approach providing significantly better results.

Key Words: Caudal epidural, lumbar interlaminar, transforaminal epidural, steroids, local anesthetic, central spinal stenosis, radiculitis

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Low back pain is the number one cause of disability (1) and lumbar spinal stenosis is one of the 3 most common diagnoses of low back and leg pain for which surgery is performed (2). Among the multitude of modalities available in managing patients with symptomatic lumbar central spinal stenosis, surgery is considered as the gold standard (2,3). However, a review of current data demonstrates a lack of consensus and wide variability in surgical decision-making for patients with lumbar spinal stenosis (4-7). Despite the continuing debate concerning outcomes, surgical interventions for spinal stenosis are increasing (3-15). Consequently, a multitude of new technologies have been developed including interspinous spacers, minimally invasive lumbar decompression (mild@ (Vertos Medical, Aliso Viejo, CA) and interventional techniques such as epidural injections and percutaneous adhesiolysis (7,16-29). In a survey of surgeons, (69%) considered epidural steroid injections to be the first-line invasive treatments for lumbar spinal stenosis after a course of conservative management has failed to provide significant relief among patients referred for surgical interventions (17). Radcliff et al (7) has opined that the high rate of epidural steroid injection use continues despite conflicting reports regarding the efficacy of this treatment in randomized controlled trials and a lack of cost effectiveness. However, their subgroup analysis provided inappropriate conclusions because of improper inclusion of the literature and a poorly designed retrospective analysis and large differences in sample sizes. Multiple systematic reviews (14,27,28,30-32), clinical trials of caudal, interlaminar, and transforaminal approaches of effectiveness (33-41) and cost effectiveness studies in managing lumbar central spinal stenosis with a caudal approach (42) have been published. In addition, multiple factors influence the outcomes of epidural injections in spinal stenosis (43-49).

Debate and controversy were sensationalized with the publication of Friedly et al's manuscript (39), accompanying editorial (50), and criticism (51). Epidural injections in the lumbar spine are administered by 3 approaches, namely – caudal, lumbar interlaminar, and lumbosacral transforaminal. Epidural injections are administered in patients after other conservative modalities of managing pain have failed, including analgesic medications, exercise, physical therapy, and/or chiropractic. Assessments of caudal epidural injections, interlaminar epidural injections, and transforaminal

epidural injections have shown mixed results in systematic reviews; however, a comparative analysis of the 3 approaches has not been performed in managing central spinal stenosis. A randomized trial comparing lumbar interlaminar and transforaminal epidural injections showed some superiority for bilateral transforaminal epidural injections in a moderate-quality trial; however, bilateral transforaminal epidural injections are associated with high risk and are not practical (52). Further, the study comparing caudal and transforaminal epidural injections is an observational study (49).

Two high-quality randomized controlled trials of caudal and interlaminar epidural injections in lumbar central spinal stenosis with 2-year follow-up with an active controlled design performed in the same setting with a similar protocol showed efficacy for both approaches with local anesthetic and steroids (34,35). In these trials, in responsive patients with at least 3 weeks of significant improvement with 2 procedures, significant improvement was seen in 54% of the patients in the caudal group compared to 84% in the interlaminar group.

This assessment is undertaken to compare the efficacy of epidural injections provided by either a caudal approach or lumbar interlaminar approach with or without steroids in providing significant improvement in patients with chronic low back and lower extremity pain secondary to lumbar central spinal stenosis. The data were compared from 2 randomized trials conducted by the same group utilizing very similar protocols and published with a 2-year follow-up in both randomized trials (34,35).

METHODS

The 2 trials included in this analysis (34,35) were conducted with a randomized, double-blind, active-control design based on Consolidated Standards of Reporting Trials (CONSORT). Both trials were performed in a private interventional pain management practice in the United States, which is a specialty referral center. The study protocols were approved by the institutional review board (IRB) and were registered with the US Clinical Trial registry with an assigned number of NCT00681447 for the lumbar interlaminar epidural injections trial and NCT00370799 for the caudal epidural injections trial.

Both trials and the present comparative assessment were conducted with the internal resources of the practice.

The patient recruitment, pre-enrollment evalua-

tion, inclusion criteria, primary interventions, additional interventions, co-interventions, objectives, outcomes, sample size determination, randomization sequence generation, allocation concealment, blinding and masking along with statistical methods and intent-to-treat analysis were described in detail in the protocols as well as the published manuscripts (34,35).

Patients

All patients were drawn from a single pain management practice for both trials. A total of 220 patients, 100 in the caudal epidural trial and 120 in the lumbar interlaminar trial, were recruited. All patients were provided with the IRB-approved protocol and informed consent.

Inclusion/Exclusion Criteria

Only patients with central spinal stenosis with lower extremity pain of at least 6 months duration were included in both studies. Patients with foraminal stenosis without central spinal stenosis, a previous history of surgery, uncontrollable medical disorders, or opioid issues were excluded.

Interventions

Of the 100 patients in the caudal trial, 50 were assigned to each group; and of the 120 patients in the lumbar interlaminar trial, 60 were assigned into each group. . Group I patients received a preservative-free local anesthetic, 0.5%, 10 mL in the caudal group and 6 mL in interlaminar group. The majority of patients randomized to included steroids were treated with non-particulate preservative-free betamethasone (6 mg in 1 mL) mixed with either 5 mL or 9 mL of 0.5% preservative free lidocaine. The solutions were indistinguishable in both groups.

All the procedures were performed under fluoroscopy by a single physician in a sterile operating room in an ambulatory surgery center with appropriate sedation. The loss of resistance technique was utilized in the lumbar interlaminar group. Contrast medium was injected in all patients.

Outcomes

Multiple outcomes were measured in both studies. These included the Numeric Rating Scale (NRS) pain scale and the Oswestry Disability Index (ODI), and other assessments. Progress was measured in all patients at 3, 6, 12, 18, and 24 months posttreatment. The NRS represents no pain with 0 and worst pain imaginable with 10

(53,54). The ODI was utilized for functional assessment on a scale of 0 – 50. The ODI represents disability as 0% to 20%: minimal disability; 20% to 40%: moderate disability; 40% to 60%: severe disability; 60% to 80%: crippled; 80% to 100%: bedbound or exaggerating their symptoms (54).

Both trials utilized significant improvement as at least 50% based on NRS and ODI scores. This is considered a robust measure compared to previous measures of a minimum clinically important difference (MCID) of 20% to 30%.

In both trials, patients responding positively with at least 3 weeks of significant improvement with the first 2 procedures were considered as successful or responsive. All others were considered as nonresponsive. Opioid intake was determined by converting to morphine equivalence.

Employment was also assessed based on various categories and employability as described in the manuscripts.

Sample Size

Sample size determination was made based on the previous assessments with the requirement of 40 patients in each group in both trials considering a power of 80%, with an allocation ratio of 1:1, and with a 10% attrition/noncompliance rate (55).

Statistical Analysis

For the present analysis, the Statistical Package for Social Sciences version 9.01 (SPSS Inc, Chicago, IL) was utilized. For categorical and continuous data comparison, Chi-square (Fisher's exact test where necessary) and t test were used, respectively. Because the outcome measures of the patients were measured at 6 points in time, the repeated measures analysis of variance (ANOVA) were performed with a post hoc analysis with Bonferroni correction. A *P* value of less than 0.05 was considered significant.

An intent-to-treat analysis, which was performed after a sensitivity analysis in the original trials, was carried forward.

RESULTS

Patient flow of 220 selected patients is shown in Fig. 1 for both trials (34,35). As described in these manuscripts, follow-up was available for 81% and 93%, in caudal and lumbar interlaminar epidural injection groups at one year and 71% and 88% at 2 years.

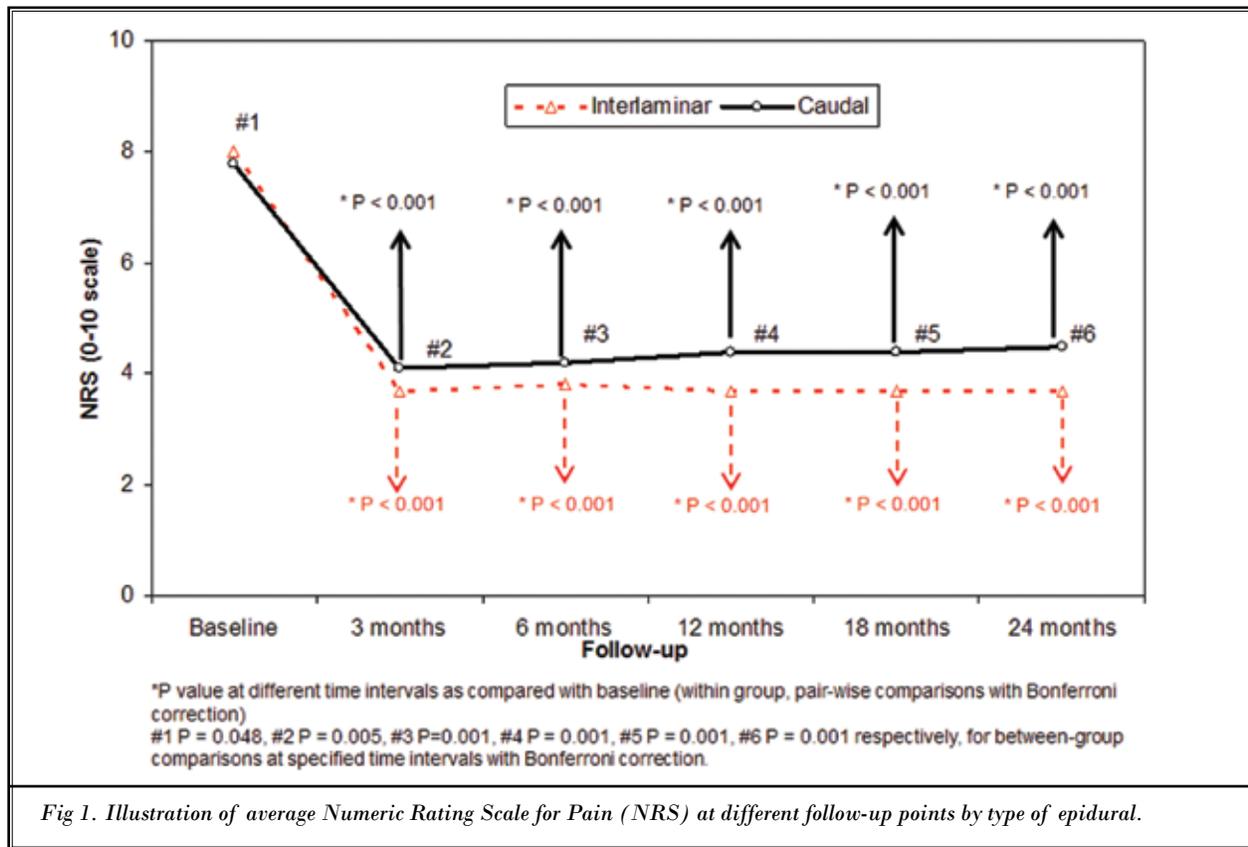


Fig 1. Illustration of average Numeric Rating Scale for Pain (NRS) at different follow-up points by type of epidural.

Table 1. Baseline demographic and clinical characteristics.

		Interlaminar (120)	Caudal (100)	P Value
Gender	Male	43% (52)	41% (41)	0.416
	Female	47% (68)	59% (59)	
Age	Mean ± SD	52.3 ± 14.6	56.3 ± 15.1	0.046
Weight	Mean ± SD	194.0 ± 48.1	191.0 ± 49.8	0.652
Height	Mean ± SD	66.9 ± 3.8	66.7 ± 3.8	0.729
Body Mass Index	Mean ± SD	30.4 ± 7.1	30.2 ± 7.7	0.811
Duration of Pain (months)	Mean ± SD	114.9 ± 92.7	99.5 ± 75.0	0.183
Onset of Pain	Gradual	80% (96)	75% (75)	0.234
	Injury	20% (24)	25% (25)	
Numeric Pain Rating Scores	Mean ± SD	8.0 ± 0.9	7.8 ± 0.9	0.047
Oswestry Disability Index	Mean ± SD	30.7 ± 7.4	29.0 ± 4.5	0.036

Recruitment

The trial recruitment period lasted from January 2007 through October 2009 for caudal epidural injections and January 2008 through May 2010 for lumbar interlaminar epidural injections.

Baseline Characteristics

There was no significant difference between the 2 groups: local anesthetic only or local anesthetic with steroid. Baseline demographic and clinical characteristics, as shown in Table 1, showed patients in the inter-

Table 2. Spinal stenosis (primary) severity and involved level(s) as classified by radiologist(s) (MRI or CT scan)

Spinal Stenosis		Interlaminar (120)	Caudal (100)	P Value
Severity*	Mild	47% (56)	30% (30)	0.039
	Moderate	36% (43)	45% (45)	
	Severe	17% (25)	25% (25)	
Levels#	L3/4	11% (13)	15% (15)	0.014
	L4/5	72% (87)	54% (54)	
	L5/S1	17% (20)	31% (51)	

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

Table 3. Comparative results of Numeric Rating Scale for Pain and Oswestry Disability Index for 2 years (Mean ± SD) of lumbar interlaminar and caudal epidural injections.

	Numeric Rating Scale for Pain		Oswestry Disability Index	
	Interlaminar (120)	Caudal (100)	Interlaminar (120)	Caudal (100)
Baseline	8.0 ± 0.9	7.8 ± 0.9	30.7 ± 7.4	29.0 ± 4.5
3 months	3.7*# ± 1.4	4.1* ± 1.9	15.2*# ± 5.7	17.0* ± 7.3
6 months	3.8*# ± 1.7	4.2* ± 1.8	14.9*# ± 6.1	17.0* ± 7.7
12 months	3.7*# ± 1.8	4.4* ± 1.9	14.7*# ± 6.4	17.2* ± 7.7
18 months	3.7*# ± 1.8	4.4* ± 1.9	14.7*# ± 6.9	17.2* ± 7.5
24 months	3.7*# ± 1.8	4.5* ± 1.9	14.4*# ± 6.9	17.3* ± 7.4
Group Difference	0.001		0.001	
Time Difference	0.001		0.001	

A lower value indicates a better condition

* significant difference with baseline values within the group (P < 0.001)

significant difference with caudal epidural group (P < 0.01)

laminar group were younger with high numeric NRS and ODI scores. Analysis showed that these differences, though significant, were mild and did not make any significant difference in the outcomes. Further, assessment of the proportion of patients with significant improvement also prevented any influence of these factors on outcome parameters.

Table 2 shows stenosis severity and levels in both trials. The prevalence of stenosis at the L4/5 levels was in more patients in the interlaminar group (72%) than the caudal group (54%).

Pain Relief and Functional Assessment

Table 3 and Figures 1 and 2 show combined results of local anesthetic only and local anesthetic with steroid in interlaminar and caudal epidural trials. Repeated measures of ANOVA revealed time × factor (P < 0.001 for both NRS and ODI), and between groups effect was significant (P < 0.001 for NRS and ODI). Follow-up

within group pair-wise analysis revealed that NRS and ODI decreased significantly at all time intervals compared with baseline (Table 3). Between-group analysis revealed that NRS and ODI scores were superior in the interlaminar trial compared to the caudal trial at all time intervals.

Significant improvement was defined as 50% or more improvement in pain relief and functional status assessment is shown in Figs. 3 – 6. As shown in Fig. 5, significant pain relief at 12 months was 73% and 45% (P < 0.001), and at 24 months was 73% and 41% (P < 0.001) for interlaminar and caudal epidurals, respectively. These results indicate the interlaminar approach to be superior to the caudal approach at all follow-up points. Figure 6 shows significant improvement for only responsive patients with 84% and 54% (P < 0.001) at 24 months for interlaminar and caudal epidurals. There was a significant difference between groups at all follow-up points.

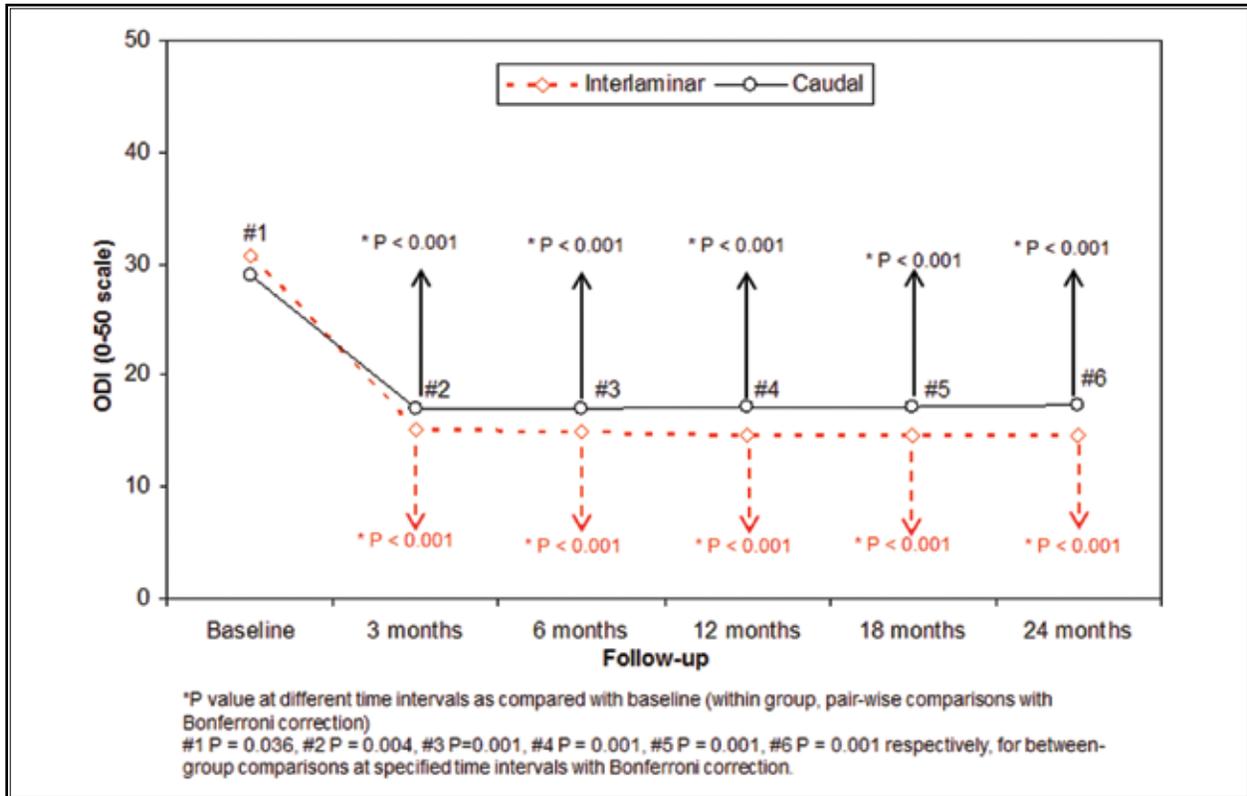


Fig 2. Illustration of average Oswestry Disability Index (ODI) at different follow-up points by type of epidural.

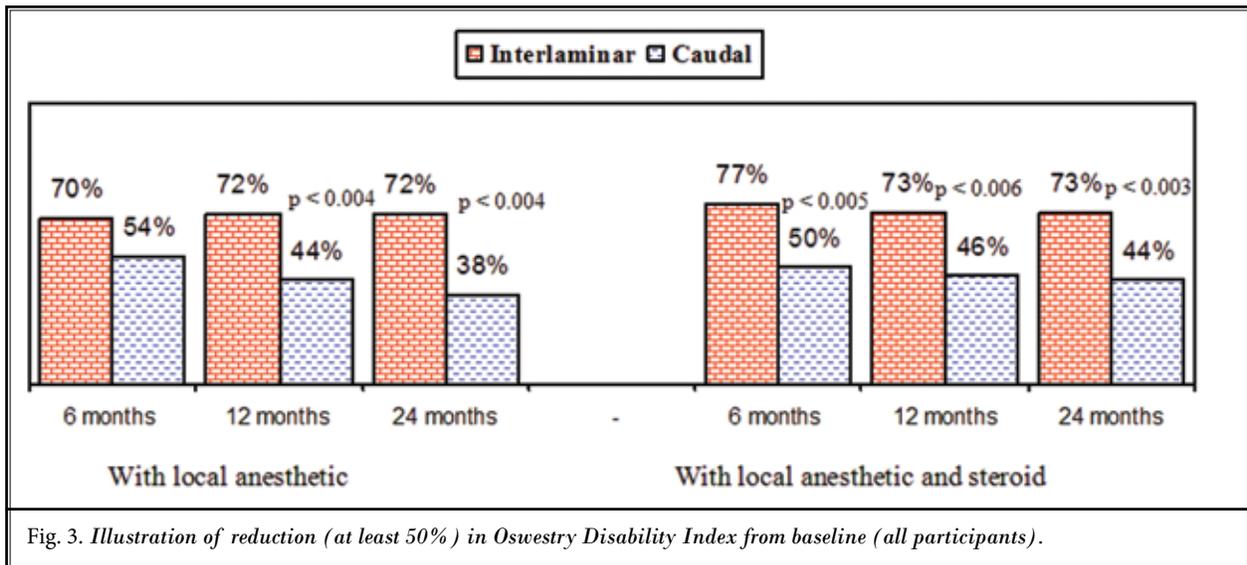


Fig. 3. Illustration of reduction (at least 50%) in Oswestry Disability Index from baseline (all participants).

Therapeutic Procedural Characteristics

Table 4 shows therapeutic procedural characteristics with the frequency over 2 years of average relief

per procedure and average total relief in weeks. These results show a significant difference for interlaminar epidural injections compared to caudal epidural injec-

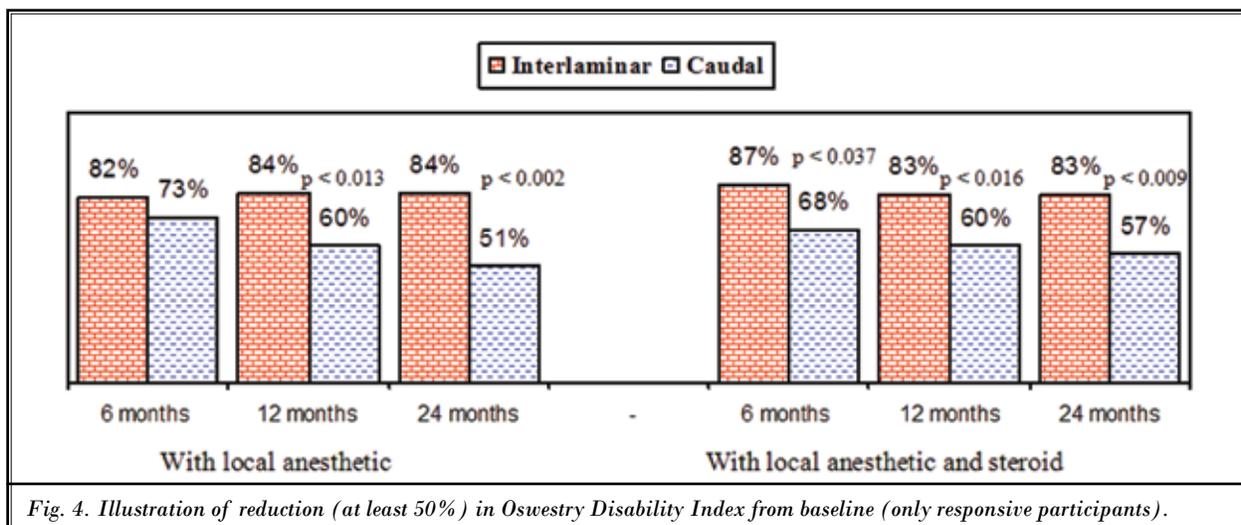


Fig. 4. Illustration of reduction (at least 50%) in Oswestry Disability Index from baseline (only responsive participants).

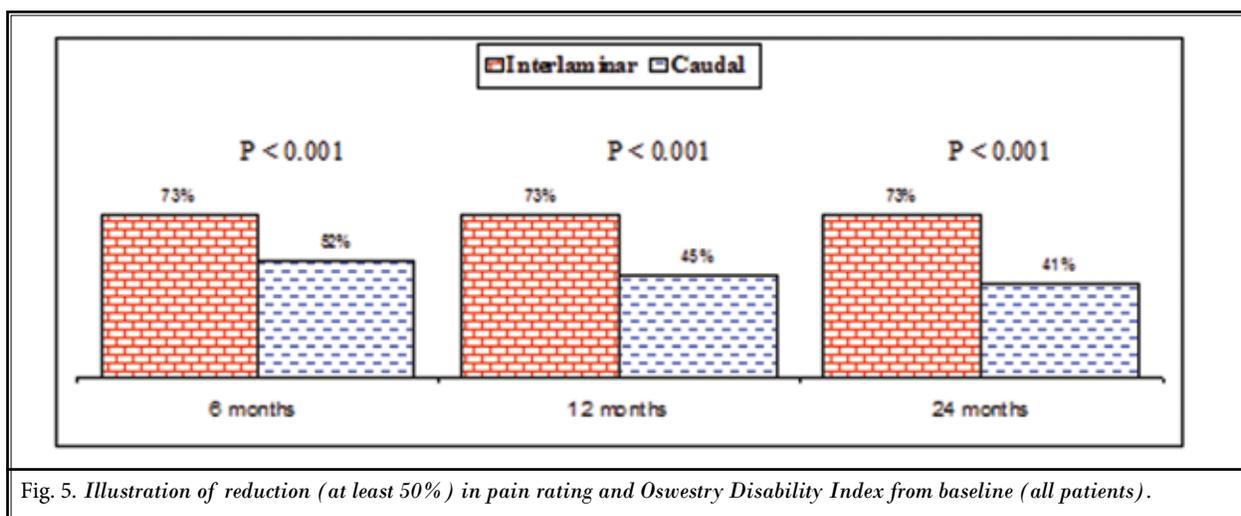


Fig. 5. Illustration of reduction (at least 50%) in pain rating and Oswestry Disability Index from baseline (all patients).

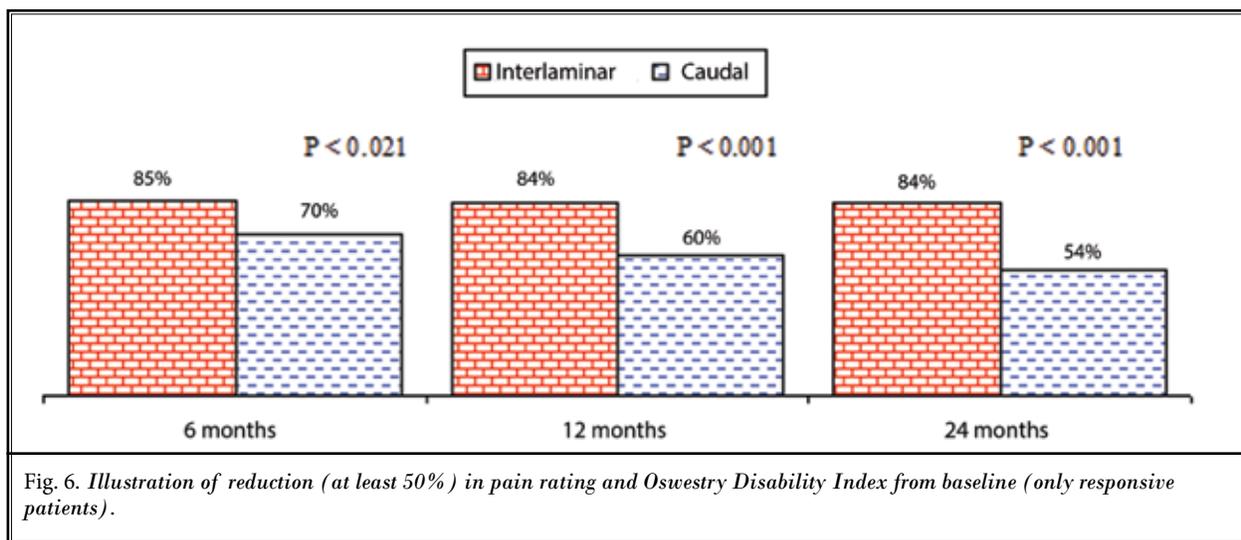


Fig. 6. Illustration of reduction (at least 50%) in pain rating and Oswestry Disability Index from baseline (only responsive patients).

tions in responsive patients as well as all patients. However, the number of procedures in the interlaminar approach was higher compared to the caudal approach.

Nonresponsive patients were higher in the caudal group compared to the interlaminar group (26 vs. 16): 26% with a caudal approach and 13% with an interlaminar approach.

Adverse Events

There were no major adverse events in any trial.

Discussion

This assessment of 2 randomized, double-blind, active-controlled trials (34,35) of local anesthetic with or without steroids in managing central spinal stenosis in 100 and 120 patients either with a caudal approach or a lumbar interlaminar approach showed the efficacy for epidural injections with both approaches at the end of one and 2 years. However, the lumbar interlaminar group response rate was significantly greater at one year (73% vs. 45%) and 2 years (73% vs. 41%). In the responsive patients, those with at least 3 weeks of significant improvement with the initial 2 procedures, 60% responded with a caudal approach whereas 84% responded with an interlaminar approach at the end of one-year and 84% versus 54% with the interlaminar approach versus the caudal approach with a significant difference in the outcomes at the end of 2 years. Both studies were performed in a contemporary interventional pain management setting. The interventions were provided as deemed medically necessary for

patients suffering with persistent, severe, chronic low back and lower extremity pain. Both trials showed significantly better improvement in the responsive category of patients compared to the nonresponsive category of patients. However, the nonresponsive category of patients, those with a lack of response of at least 3 weeks with the 2 initial procedures, was significantly higher in the caudal epidural group (29%) compared to the lumbar interlaminar epidural group (13%). There were no differences in outcomes based on the severity or level of stenosis.

These results of caudal epidural injections may not be compared with any other trial as there are no other randomized trials assessing the role of caudal epidural injections in central spinal stenosis of the lumbar spine. Further, the trial describing the caudal approach is a high-quality trial with long-term follow-up.

Caudal epidural injections may be limited with spread of injectate above S1 in some patients. In these trials (34,35) stenosis was present at L4/L5 levels in 86 of 120 patients or 72% in the interlaminar group and 54 of 100 patients or 54% in the caudal epidural group. Radcliff et al (7) also showed L4/L5 involvement in over 90% of patients. Thus, it appears that because of the restricted flow patterns in caudal epidural injections, which may not reach the target level, thus if the stenosis is at L4/L5 a lumbar interlaminar epidural may be more effective since the injection is being provided close to the pathology.

In reference to interlaminar epidural injections, there are multiple moderate- or low-quality trials sup-

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

	Responsive Patients		Non-responsive Patients		All Patients	
	Interlaminar (104)	Caudal (74)	Interlaminar (16)	Caudal (26)	Interlaminar (120)	Caudal (100)
Average Number of Procedures for One Year	3.7 ± 1.0	3.5 ± 1.1	1.9 ± 0.7	1.5 ± 0.6	3.5* ± 1.2	3.0 ± 1.4
Average Number of Procedures for 2 Years	5.9* ± 2.4	4.8 ± 2.4	1.9 ± 0.7	1.7 ± 1.1	5.4* ± 2.6	4.0 ± 2.6
Average Relief for First Procedure	6.6 ± 10.5	7.1 ± 12.7	0.9 ± 1.1	1.2 ± 2.0	5.9 ± 9.9	5.5 ± 11.3
Average Relief for Second Procedure	12.1 ± 15.9 (103)	11.1 ± 14.9 (73)	0.6 ± 0.8 (12)	0.8 ± 1.7 (12)	10.9 ± 15.5 (115)	9.7 ± 14.3 (85)
After initial 2 Procedures	15.6 ± 12.5 (406)	13.7 ± 8.9 (210)	0.5 ± 0.5 (3)	10.2 ± 5.8 (5)	15.4 ± 12.5 (409)	13.6 ± 8.8 (215)
Average Relief per Procedure	13.5* ± 13.2 (613)	11.8 ± 11.5 (357)	0.7* ± 0.9 (31)	2.1 ± 3.9 (43)	12.8* ± 13.2 (644)	10.8 ± 11.3 (400)
Average Total Relief for One Year (Weeks)	40.4* ± 12.1	32.9 ± 16.8	1.4 ± 1.3	2.0 ± 3.6	35.2* ± 17.4	24.8 ± 19.9
Average Total Relief for 2 Years (Weeks)	77.4* ± 28.9	56.9 ± 39.3	1.4 ± 1.3	3.5 ± 11.1	67.3* ± 37.4	43.1 ± 41.5

*Significant difference with caudal epidurals

porting the efficacy of interlaminar epidural injections in managing central spinal stenosis (35,37-41), whereas one recent high profile trial by Friedly et al (39) and accompanying editorial contradict the results of the interlaminar trials. However, the trial by Friedly et al (39) and the editorial by Andersson (50) have been criticized extensively for their design, quality of literature search, omission of multiple randomized trials including the randomized trial included in this analysis, the mode of outcomes assessment, outcomes assessments parameters, inclusion of acute pain patients, performance of procedures with variable volumes of injectate, and the conclusion that there is a lack of efficacy even though the results clearly show that both approaches, interlaminar and transforaminal, were effective with local anesthetic only or with local anesthetic with steroids, with the interlaminar approach showing potential superiority. Similar issues prevailed with the other trial by Radcliff et al (7) with poor subgroup analysis and reporting. The systematic reviews by Kovacs et al (18), Ammendolia et al (27), and Bresnahan et al (28) also faced significant criticism for poor search criteria and inappropriate analysis leading to conclusions not based on evidence (56). However, systematic reviews utilizing appropriate methodology and evidence synthesis have arrived at appropriate conclusions showing moderate efficacy for caudal and lumbar interlaminar epidural injections in managing central spinal stenosis (16,30,32). Thus far there has not been any comparative analysis performed in a single study or comparison of multiple randomized trials comparing various approaches in managing central spinal stenosis. Considering the multiple risks associated with multilevel, bilateral transforaminal epidural injections, it appears that caudal and interlaminar approaches are appropriate.

This assessment may be criticized for the inclusion of 2 separate randomized trials in analyzing the data with both of them being active-controlled trials rather than placebo-controlled trials. In the era of evidence-based medicine and comparative effectiveness research, practical clinical trials with a pragmatic approach are considered to be clinically applicable and valid (57-59). Placebo controlled trials, the definition of true placebo, the influence of placebo and nocebo, and the design of true placebo controlled trials in interventional pain management have been extensively discussed (60-63). Thus, the trials utilized in this assessment met the essential criteria for practical clinical trials, with measurement of effectiveness, rather than efficacy, which is considered as more clinically appli-

able in interventional pain management (57-59,63-65). The deficiency of this assessment of including 2 separate trials may be appropriate at this time as there have not been any randomized trials comparing caudal and interlaminar epidural injections. Further, a widely publicized trial from the New England Journal of Medicine by Friedly et al (39), even though it included a large proportion of patients and compared lumbar interlaminar and transforaminal epidural injections, was unable to provide any practical information as the assessments were completed at 6 weeks which is inappropriate for interventional techniques which require at least 6 to 24 months of follow-up and was associated with inappropriate conclusions which were not based on the reported results. Further, blinding would be extremely difficult if a trial were performed comparing caudal and interlaminar approaches. Finally, multiple systematic reviews which have equated local anesthetic with placebo have reached inappropriate conclusions (29,66-68). Properly conducted trials have shown the appropriate effect of sodium chloride solution with injection into an inactive structure(s) (64,65). There has been ample evidence demonstrating the various clinical effects produced by injecting inactive substances into active structures (62,69-73).

Epidural injections with steroids have been used to treat central spinal stenosis as well as disc herniation and radiculitis and foraminal stenosis based on the pathophysiologic mechanism of inflammation (16). Epidural steroids have been shown to be effective in disc herniation and radiculitis, as well as spinal stenosis secondary to their antiinflammatory properties (42,74). In recent years, emerging evidence also has shown that local anesthetics without steroids are equally effective as local anesthetics with steroids in many settings (73). This analysis shows no significant difference between local anesthetic only or local anesthetics with steroids with caudal and interlaminar approaches.

In summary, this analysis comparing 2 high-quality randomized trials shows the effectiveness for both local anesthetics only or local anesthetics with steroids with caudal and lumbar interlaminar approaches; however, this analysis also shows the superiority of interlaminar epidural injections with local anesthetic only or local anesthetic with steroids compared to a caudal approach.

CONCLUSION

The results of a 2 year follow-up of 2 randomized, double-blind, active-controlled trials, with 220 patients with chronic persistent pain of central spinal stenosis

receiving either caudal epidural or lumbar interlaminar epidural injections with local anesthetic only or local anesthetic with steroids showed efficacy for both techniques and superiority for lumbar interlaminar epidural injections.

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