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Efficacy of Steroid and Nonsteroid Caudal Epidural Injections for Low Back Pain and Sciatica

A Prospective, Randomized, Double-Blind Clinical Trial

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Study Design. Prospective, double-blind, randomized, case-control study.

Objective. To evaluate the efficacy of caudal epidural injections (CEI) containing steroid *versus* nonsteroid preparations when treating patients suffering from low back pain (LBP) and sciatica.

Summary of Background Data. Literature seems to be deprived of well-designed randomized, controlled studies that evaluate the effectiveness of CEI in the treatment of chronic LBP; hence the value of CEI remains still the subject of controversy.

Methods. Patients suffering from severe chronic LBP and sciatica were randomly allocated into 2 groups. Steroid-group's patients (n = 93) underwent CEI containing 12 mL of xylocaine 2% and 1 mL of betamethasone dipropionate and betamethasone phosphate (2 + 5) mg/dL. Water for Injection (WFI)-group's patients (n = 90) underwent CEI containing 12 mL of xylocaine 2% and 8 mL of WFI. Both groups were statistically comparable as far as their demographic data and the cause and duration of symptoms were concerned. Patients answered the Oswestry Disability Index questionnaire and underwent physical examination, before and at 1 week, 1 month, 6 months, and 1 year following the CEI.

Results. Symptoms improved in 132 patients (72.1%) following CEI. The mean Oswestry Disability Index questionnaire score of steroid-group's patients was statistically significant lower than that of the WFI-group at all postinjection re-evaluations. Patients receiving steroid CEI experienced faster relief during the first postinjection week. The Straight Leg Rising test improved in both groups following CEI; this improvement was faster among steroid-group's patients. Fifty-one patients (27.8%), noticed no improvement 1 week post-CEI and underwent a second CEI (with the same preparation) 7 to 14 days later. Nineteen of them reported improvement; 32 (steroid-group:13, WFI-group:19) did not respond well and underwent operative decompression (n = 15) or spinal fusion (n = 17).

Conclusion. CEI containing local anesthetic and steroids or WFI seems to be effective when treating patients with LBP and sciatica. CEI containing steroid preparations demonstrated better and faster efficacy.

Key words: low back pain, sciatica, caudal epidural injection, caudal extradural injection, steroids, randomized double blind study. **Spine 2009;34:1441–1447**

Even though chronic low back pain (LBP) is currently estimated to affect around 15% of the US population,[1] identifying its actual cause(s) can be an extremely difficult task. Lumbar disc herniation seems to be one of the most frequent causes of LBP, nevertheless it is well known that many patients, complaining of LBP as well as of radiating leg pain suggesting sciatica, did not show lumbar disc herniation in magnetic resonance imaging (MRI) and Computed Tomography.[2] There is emerging evidence suggesting that this "paradox" must be probably attributed to the fact that nerve root compression is not sufficient by itself to cause nerve root pain,[3] since painful radiculopathy may be the end-result of a local chemical contribution from injured tissue.[4] Treating patients suffering from LBP can also be challenging and this is probably why so many treatment methods (ranging from conservative measures to operations) have been introduced and are supported by the literature.[2]

Ever since its introduction, the value of caudal epidural injection (CEI) when managing spinal pain and sciatica, has been the subject of controversy.[1,5,6] Literature moderately supports the use of CEI containing steroid preparations for the long-term relief of patients suffering from chronic LBP,[7] even though there seems to be a lack of relevant well-designed randomized, controlled studies. The actual effect(s)—if any—and the mode(s) of action of CEI (containing steroids or not) on patients with chronic LBP, remain more or less unknown.[7,8] Aim of this study was the evaluation of the efficacy of CEIs containing local anesthetic and either steroid or water for injection (WFI) as a means of treatment for patients suffering from severe chronic LBP and sciatica.

Materials and Methods

This prospective, randomized, double-blind, case-control study was approved by our institution's Scientific Research Board and was conducted in accordance with the World Medical Association Declaration of Helsinki of 1964 as revised in

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This study has been approved by the Institution's Review Board and was conducted in accordance with the World Medical Association Declaration of Helsinki of 1975, as revised in 1983. After the patients (where applicable) were fully informed, they consented that data concerning their cases could be submitted for publication.
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1983 and 2000. All patients were informed about their participation in the study and gave informed consent.

Between September 2005 and June 2007, a group of 191 patients suffering from persistent LBP for a period of at least 1 month (with or without unilateral or bilateral sciatica) not responding well to conservative pain control measures,[5] were offered enrollment in the study. All patients had undergone MRI scans confirming the existence of lumbar disc related pain (disc degeneration or herniation) that was expected to improve following a CEI. Patients were offered the opportunity to continue their treatment with conservative measures and/or undergo an operation instead of participating in the study. A positive Straight Leg Rising (SLR) test was not considered as mandatory in order a patient to be enrolled in the study, since it is well accepted that degenerative changes do not necessarily correlate with pain generation. Patients reporting symptoms and/or signs of *cauda equina* or spinal stenosis, experiencing symptoms for a period of less than a month, or suffering from psychosomatic diseases or any other pathology were excluded. None had participated in a similar study or undergone any CEI.

Following screening and enrolment (visit 1), all patients were physically examined, answered the Oswestry Disability Index questionnaire (ODI)[9] and were randomized into either the steroid or the "WFI-group." Steroid-group's patients underwent CEI with 12 mL of xylocaine 2% and 1 mL of betamethasone dipropionate and betamethasone phosphate (2 + 5) mg/dL; WFI-group's patients with 12 mL of xylocaine 2% and 8 mL of WFI.

All CEIs were performed by the same physician/author who was blinded to each patient's enrollment status. In order to eliminate bias as much as possible, all syringes (containing the appropriate preparation for each patient) were prepared by a different physician/author and were given to the physician performing the CEI wrapped in a nontransparent cover. Following skin preparation, the sacral hiatus was identified and both the skin overlying the sacral hiatus and the underlying ligaments were infiltrated with local anesthetic. Patients underwent blinded CEI with the use of a spinal needle (Becton Dickinson 19 or 21 gauge). Gentle aspiration confirmed the proper position of the needle. Following CEI, each patient remained at the outpatient clinic for a period of 30 to 60 minutes and until he/she felt physically and psychologically fit to be discharged. Patients were allowed to receive paracetamol but not nonsteroid-anti-inflammatory drugs during the first 4 weeks of the study.

Clinical evaluations were performed (by physicians/authors that were blinded to the group that each patient belonged to) at 1 week (visit 2), 1 month (visit 3), 6 months (visit 4), and 1 year (visit 5) following the CEI. The ODI score[6] and the Straight Leg Rising (SLR) test (positive $<60°$) were used to differentiate patients whose symptoms improved from those who remained symptomatic.

Based on results published in similar randomized trials,[10,5] it was demonstrated that with a sufficient power of 0.90 and α value of 0.05, in order to see a difference of 5° in the ODI score between the 2 groups and with an overall standard deviation assumed to be 8°, at least 60 patients had to be enrolled in each arm/group of the study. Standard statistical methods were used for descriptive statistics. The Kolmogorov-Smirnov test evaluated the normality of the data distribution among different groups. All statistical tests were 2-tailed. The alpha level for all analyses was set at 0.05. An independent sample *t* test or Mann-Whitney *U* test determined the significance of the differences found in the mean ODI scores between the 2 groups at different follow-up periods. The Wilcoxon Signed Ranks test determined the significance of the differences found in the mean ODI score among patients of the same group at different follow-up evaluations. χ^2 test was used to compared the number of patients with positive or negative SLR tests between the 2 groups. Kaplan-Meier survival curves determined the probability of having a negative SLR test in each group following CEI. The SPSS statistical software (Version 12, Chicago-IL) was used.

Table 1. The Demographic and Clinical Data of the Patients

	Steroid-Group	WFI-Group	*P*
Age (yr)*	50.75 (15.52)	47.56 (16.42)	0.179†
Sex			
Men‡	60	63	0.527§
Women‡	33	27	
Symptoms that patients had at examination before caudal injection			
Back pain + unilateral leg pain¶	41 (44%)	33 (36.6%)	0.514§
Back pain + bilateral leg pain¶	18 (19.3%)	17 (18.8%)	
Back pain only¶	34 (36.5%)	40 (44.4%)	
Symptoms duration before CEI (d)*	53.1 (33.5)	51.4 (30.4)	0.680‖
ODI before injection*	38.5 (2.64)	38.5 (2.7)	0.746‖
Magnetic Resonance Imaging Diagnosis			
Disc Degeneration‡	51	57	0.243§
Disc Herniation‡	42	33	

*The values are given as the mean with the standard deviation in parentheses.
†Tests performed using independent sample *t* test.
‡The values are given as raw numbers.
§Tests performed using $\chi 2$ test.
¶The values are given as raw numbers with the percentages in parentheses.
‖Tests performed using Mann-Whitney *U* test.

Results

One hundred eighty-three patients (steroid-group:93, WFI-group:90) were enrolled (mean age:49.3 ± 15.6 years). The 2 groups were comparable (age of patients, male/female ratio, type and duration of symptoms, ODI scores before CEI, and radiographic and MRI findings) (Table 1).

No patient reported any major immediate or late complication(s) following CEI. Twenty patients (steroid-group:12, WFI-group:8) reported experiencing transient bilateral lower extremity numbness immediately after the CEI. Another 12 (steroid-group:5, WFI-group:7) felt as if they were going to faint; however, their blood-pressure and pulse rate were normal in all cases. None reported any lower limb dysfunction in terms of loss of sensation and/or reduced motor power, or bladder and bowel dysfunction(s).

At the first follow-up visit (visit 2), 51 patients noticed no improvement of their symptoms. They all underwent a second CEI during the week following visit 2, with the same preparation that was initially used. Nineteen reported improvement after that. Thirty-two however, (steroid-group:13, WFI-group:19, χ^2 test, $P = 0.204$)

Table 2. Comparison of the Mean ODI Scores Between Steroid- and WFI-Groups' Patients at all Postinjection Follow-up Periods

	Groups	N	Mean	SD	*P*
ODI	Steroid-group	93	12.1	13.1	0.000
1 wk after injection	WFI-group	90	29.9	6.2	
ODI	Steroid-group	89	8.7	11.9	0.000
1 mo after injection	WFI-group	85	23.5	9.6	
ODI	Steroid-group	83	5.8	8.6	0.000
6 mo after injection	WFI-group	70	13.6	10.5	
ODI	Steroid-group	81	4.91	7.05	0.000
1 yr after injection	WFI-group	70	13.00	10.14	

N indicates the number of patients examined at each visit minus those who had been operated on until then; SD, standard deviation.

Table 3. Comparison of the Mean ODI Scores Between Adjacent Follow-up Periods of Patients Enrolled in the Steroid- and WFI-Groups Separately

	Wilcoxon Signed Ranks Test Asymptomatic Significance (2-Tailed)	
ODI (Mean Value)	Steroid-Group	WFI-Group
Preinjection + 1 wk	0.000	0.000
1 wk + 1 mo	0.000	0.000
1 mo + 6 mo	0.072	0.000
6 mo + 1 yr	0.288	0.000

had no improvement in their symptoms after the second CEI as well and decided to be operated on. Patients suffering from disc herniation (steroid-group:7, WFI-group:8) underwent decompression, whereas patients suffering from LBP due to motion segment dysfunction (steroid-group:6, WFI-group:11) underwent spinal fusion. These subgroups of patients that were operated on were statistically comparable as far as the findings in the MRI scans were concerned (χ^2 test, $P = 0.456$).

The patients' mean ODI scores kept decreasing (representing improvement of their symptoms) at all follow-up re-evaluations in both groups (Table 2, Figure 1). The mean ODI score of the steroid-group was statistically significantly lower, when compared with the score of the WFI-group, at all post-CEI visits (Table 2). The observed decreases of the mean ODI scores of steroid-group's patients, (a) between visit 1 and 2, and (b) between visit 2 and 3, were statistically significant (Table 3). There was also a decrease (but not statistically significant) of the mean ODI scores of the steroid-group's patients between visit 3 and 4 and visit 4 and 5 (Table 3). The Wilcoxon Signed Ranks test showed statistically significant differences in the observed decreases of the mean ODI scores of the WFI-group, between all pairs of "adjacent" visits (Table 3).

Starting at visit 2 and continuing until visit 5, the SLR test kept improving in both groups. No statistically significant difference was noted in the number of patients with bilateral, unilateral, positive or negative SLR test between the 2 groups from visit 2 until visit 5, with the exception of visit 3 (Table 4).

Kaplan-Meier analysis showed that the mean time necessary in order the SLR of the patients belonging to the steroid-group to become negative, was statistically

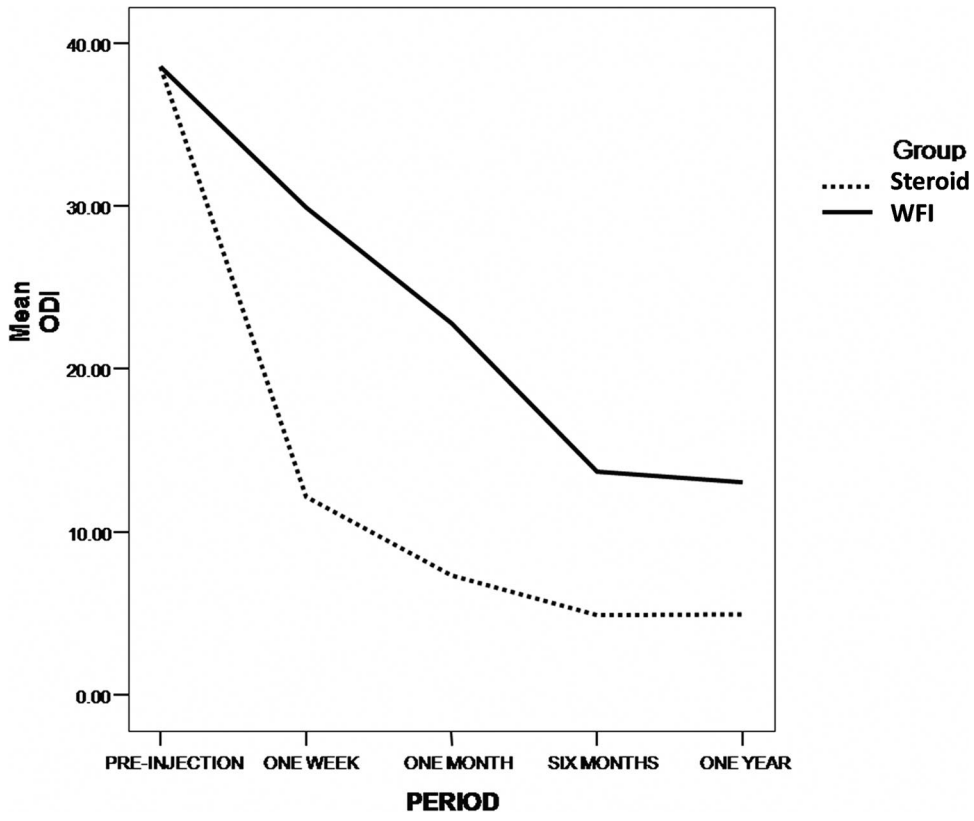

Figure 1. The Mean ODI scores of patients enrolled in both groups and at all post injection periods. The decrease of the mean ODI scores in the steroid-group's patients was greater and faster when compared with the WFI-group's results. The main therapeutic result of caudal injection in the steroid-group was apparent during the first week; hence there was an abrupt decrease in the mean ODI scores of this group's patients. WFI-group's patients had a more gradient and not so remarkable relief of symptoms.

Table 4. Patients' Symptoms During the Postinjection Period*

	Preinjection Period		1 wk Postinjection		1 mo Postinjection		6 mo Postinjection		1 yr Postinjection	
	Steroid Group	WFI Group	Steroid Group	WFI Group	Steroid Group	WFI Group	Steroid Group	WFI Group	Steroid Group	WFI Group
Unilateral SLR	41	33	23	25	15	26	3	5	1	3
Bilateral SLR	18	17	12	17	6	13	2	4	1	3
SLR negative	34	40	58	48	68	46	78	61	79	64
P	0.514		0.398		0.008		0.340		0.248	

Improvement of the Straight Leg Raising Test (SLR) sign was noted in both groups. $\chi 2$ test analysis showed no significant difference in the number of patients with bilateral, unilateral positive or negative SLR tests between the groups at all follow-up periods with the exception of 1 month after caudal injection.
*Operated patients are not included in this table.

significant less than that of the WFI-group (log-rank test, $P = 0.000$) (Table 5). Patients enrolled in the steroid-group were much more likely to have a negative SLR test following CEI, when compared with the WFI-group's ones (Figure 2).

■ Discussion

Even though the prevalence of persistent LBP (with or without radicular pain) is high and the morbidity accompanying it is substantial,[11] its etiology remains controversial.[12] There is increasing evidence that an intervertebral disc can contribute to LBP through various processes (degeneration, herniation, inflammatory reactions).[8] These processes are related to a series of morphologic and biochemical changes and their combination seems to alter the mechanical properties of the motion segment.[8]

Sicard introduced, in 1901, the injection of cocaine through the sacral hiatus into the epidural space, in order to treat patients suffering from severe, intractable sciatic pain or lumbago.[10,12] Ever since, CEIs are commonly used when dealing with chronic low back and/or radicular pain[8] in order to address potential pathology adjacent to the epidural space.

The caudal approach to the epidural space is the earliest known technique for epidural steroid injection or blocks.[13] This approach however, did not gain universal recognition until 1925, when Viner popularized its use for the treatment of sciatica.[13] Evans was the first to report good results in patients undergoing CEI containing only saline[12]; he attributed them to the physical displacement of the neuronal elements and to the stretching and lysis of the neuronal adhesions caused by the injectate.[11]

Numerous studies tried to evaluate whether CEI is an efficient method when treating patients suffering from LBP and/or sciatica. Unfortunately, most of them were performed by multispecialty physicians, are deprived of proper methodology and statistical analysis and report results often contradictory and confusing.[12] Extensive literature research revealed only 4 randomized, double-blind prospective studies assessing the efficacy of CEI.[5] Dansfield *et al*[14] evaluated 60 patients suffering from chronic sciatica (duration >6 months). Patients received epidural injections (containing 10 mL of lidocaine 1% with triamcinolone 40 mg) either caudally or over the nerve root *via* epiduroscopy. Both treatments were effective and no significant differences were found. Breivik *et al*[5] evaluated 35 patients suffering from chronic LBP and sciatica. Patients received up to 3 weekly CEIs containing bupivacaine and either methylprednisolone or saline. During the initial post-CEI period, there was a significant difference between the 2 groups (favoring the steroid-group) as far as the relief of symptoms and return to work were concerned. Bush and Hillier[10] evaluated 23 patients with chronic sciatica. Patients underwent CEI containing triamcinolone acetonide either with procaine hydrochloride 0.5% or saline. The short-term results (concerning pain relief and mobility) favored significantly the steroid-group. In the long-term however, results were similar between the 2 groups, as far as pain relief was concerned. Matthews *et al*[12] compared the results of 57 patients suffering from sciatica (mean duration of symptoms: 4 weeks) treated with CEIs containing either bupivacaine and methylprednisolone acetate or lignocaine. The authors reported negative short-term and positive long-term relief in favor of the steroid-group.

We assessed and compared the efficacy of CEIs containing a preparation of local anesthetic and steroid or WFI in 2 (statistically comparable) groups of patients with chronic LBP and sciatica. The number of patients enrolled reached and surpassed the statistically precalculated target. Our results showed that 132 patients (72.1%) from both groups responded well to the first CEI. Recovery from symptoms was steadily observed from the first week following CEI in both groups. How-

Table 5. The Kaplan-Meier Survival Analysis Statistics

	Survival Time (wk)	Standard error	95% Confidence Intervals	Long Rank Test		
				$\chi 2$	*P*	*df**
Steroid Group						
Mean	26.3	1.4	23.5–29.1	20.07	0.000	1
Median	24	2.4	19.1–28.8			
WFI group						
Mean	35.2	1.5	32.2–38.2			
Median	48	1.7	44.4–51.5			

**df* indicates degrees of freedom.

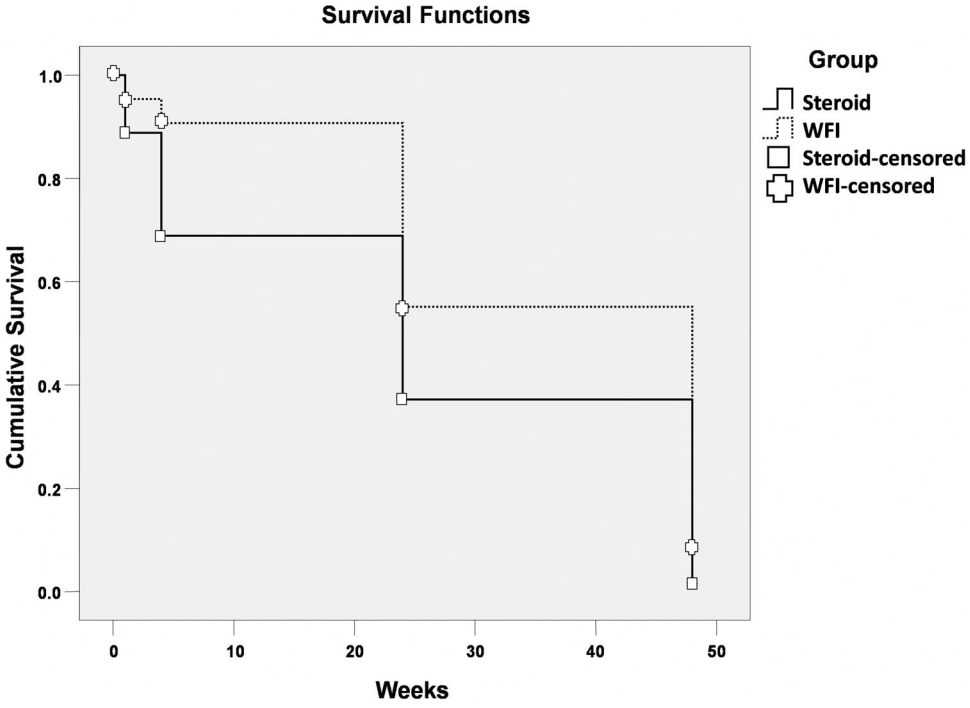

Figure 2. The Kaplan-Meier survivor probability curve of both groups. Each curve separately indicates the probability of having a negative SLR test over time for each group. Patients enrolled in the steroid-group were much more likely to have a negative SLR test after caudal injection. Day 1 indicates the time of caudal injection.

ever, the rate of decrease in the ODI score was faster and greater in the steroid-group (Figure 1). Furthermore, the main therapeutic result of CEI in the steroid-group appeared during the first week, when immediate decrease in the mean ODI score of the patients was noticed (Figure 1). WFI-group's patients noticed a more gradient and less considerable relief from their symptoms (Figure 1). In addition, steroid-group's patients were much more likely to have a negative SLR test following CEI, thus showing faster improvement as far as leg pain was concerned (Figure 2).

Our results support the existence of both short- and long-term relief from symptoms for both groups. However, CEIs containing steroid preparations seem to act faster and more efficiently, especially when considering the fact that most similar studies involve multiple CEIs. This should probably be attributed either to the shorter duration of symptoms, or to the preparation used (or both). Literature research failed to retrieve any study involving the use of betamethasone when treating patients suffering from LBP and/or sciatica with CEI. However, the epidural injection of betamethasone in a model of lumbar radiculopathy showed a significant effect on thermal hyperalgesia.[15]

All our patients had MRI confirmation of lumbar disc-related pain.[8] Although it has been suggested that inflammatory reactions between the nucleus pulposus and nerve roots are playing a crucial role in relating disc herniation to sciatica, the exact pathogenetic mechanisms are still not clear.[16–28] A high level of phospholipase A2 activity may initiate the inflammation of sensory neurons in the affected associated dorsal root ganglions. Although the efficacy of CEI in the treatment of LBP and sciatica has been clearly demonstrated, appropriate explanations for such benefits continue to lack scientific validity.[14,29,30] Corticosteroids probably exert their anti-inflammatory actions either by inhibiting the synthesis or release of a number of pro-inflammatory substances or by causing a reversible local anesthetic effect.[14,29,30] Membrane stabilization, inhibition of neural peptide synthesis or action, blockade of phospholipase A2 activity, prolonged suppression of ongoing neuronal discharge and suppression of sensitization of dorsal horn neurons are also possible actions exerted by corticosteroids.[12] In addition, the administration of epidural solutions clears or dilutes the locally concentrated chemical irritants around the spinal nerve roots[10]; hence the introduction of saline in the epidural space may exert an independent therapeutic action. This may be a possible explanation for the improvement seen in the WFI-group. Nevertheless, the reader must be aware that (as reported in several studies comparing the efficacy of operative *versus* conservative treatment for lumbar disc herniation and sciatica[31,32]) the long-term relief from symptoms that the majority of this study's patients felt, may be the end-result of the natural course of the disc-herniation itself and not the outcome of this particular or other intervention(s).

As advantages of our study should be considered the large number of patients enrolled, the use of a validated questionnaire (ODI) as an outcome measure (instead of more subjective criteria such as returning to work or a visual analogue scale) and the detailed statistical analysis.

This study however, has also certain limitations. CEIs were performed without fluoroscopic guidance, which is the gold standard for accurate needle placement.[33] Nonetheless, there are several methods that can be

used when trying to achieve the proper placement and confirmation of the right position of the needle in the sacral hiatus without fluoroscopic guidance.[34,35] Successful CEI without fluoroscopic guidance may be achieved by these methods in 92% of cases. Stitz and Sommer support that the rate of success (when placing the needle in the sacral hiatus) is high, as long as readily palpable anatomic landmarks are properly recognized.[36]

Another limitation was the fact that the SLR test was used in terms of reviewing patients. It is true that SLR test's results largely depend on each patient's flexibility. This is a reason why a large number of patients had a negative SLR at visit 1 (Table 4). Nevertheless, we believe that setting the threshold of a positive SLR test at 60° is a justified compromise. Furthermore (and even though the SLR test should probably be considered as an indirect way of palpating tissues which are sensitive such as the nerve root in the case of sciatica, or the dura in the case of lower back pain) it still is more objective than each patient's reports of pain. A last but not least issue concerning the SLR was the fact that all relative results concerning tests between adjacent re-evaluations were used in order to evaluate the efficacy of CEIs and not to associate the SLR test itself with LBP or sciatica.

Our article would have probably been better if we had included a third group of patients undergoing CEIs with local anesthetic only. This type of CEI however, would probably offer only temporary relief; hence we decided against it. This is also the reason why WFI-group's patients underwent CEIs containing 8 mL of WFI (in order to assess the efficacy of the "dilutional" properties of CEIs) instead of 1 mL that would render this group into an actual "control-group."

CEI is a simple, rapid, and easily performed (at the outpatient clinic) procedure that can offer significant pain relief. CEI may even be considered as an alternative to operative procedures in patients not responding well to conservative treatment, of high operative risk, or when they refuse to be operated on. Following injection, patients are discharged, thus avoiding long periods of hospitalization and bed rest. The combination of local anesthetics with steroids and saline could be of an additional benefit; this however, remains to be proved.

CEIs containing local anesthetic and steroid or WFI could be effective in relieving the symptoms of patients suffering from LBP and sciatica. The injection of steroid with local anesthetic leads to greater and faster relief during the first week after the CEI and this improvement is maintained even 1-year later. The clinical symptoms of the WFI-group patients are relieved in a more progressive way and not as much and as fast as of the steroid-group's patients, even 1 year after the CEI. More studies are certainly needed in order to better understand the potential action of steroids or only WFI when treating patients with LBP and sciatica with CEI.

■ Key Points

- The value of CEI, as a means of spinal pain management, remains still the subject of controversy.
- Literature seems to be deprived of well–designed randomized, controlled studies that evaluate the effectiveness of CEI in the treatment of chronic LBP and sciatica.
- One hundred eighty-three patients suffering from severe chronic LBP and sciatica were randomly assigned into 2 groups and underwent CEI containing local anesthetic and either steroid or WFI.
- CEI containing either preparation seemed to be effective in managing the patients' symptoms (exerting probably different therapeutic actions).
- CEI containing local anesthetic and steroid acts in a faster way offering greater relief from symptoms while local anesthetic and WFI act more progressively and lead to a less notable improvement.

References

1. Manchikanti L, Pampati V, Rivera JJ, et al. Caudal epidural injections with sarapin or steroids in chronic low back pain. *Pain Physician* 2001;4:322–35.
2. Peng B, Wu W, Li Z, et al. Chemical radiculitis. *Pain* 2007;127:11–6.
3. Mulleman D, Mammou S, Griffoul I, et al. Pathophysiology of disc-related sciatica. I–Evidence supporting a chemical component. *Joint Bone Spine* 2006;73:151–8.
4. Kawakami M, Tamaki T, Hayashi N, et al. Possible mechanism of painful radiculopathy in lumbar disc herniation. *Clin Orthop Relat Res* 1998;351: 241–51.
5. Abdi S, Datta S, Trescot A, et al. Epidural steroids in the management of chronic low spinal pain: a systematic review. *Pain Physician* 2007;10:185–212.
6. Boswell MV, Shah RV, Everett CR, et al. International techniques in the management of spinal pain: evidence based practice guidelines. *Pain Physician* 2005;8:1–47.
7. Abdi S, Datta S, Lucas LF. Role of epidural steroids in the management of chronic spinal pain: a systematic review of effectiveness and complications. *Pain Physician* 2005;8:127–43.
8. Boswell MV, Hansen HC, Trescot AM, et al. Epidural steroids in the management of chronic spinal pain and radiculopathy. *Pain Physician* 2003;6: 319–34.
9. Boscainos PJ, Sapkas G, Stilianessi E, et al. Greek versions of the Oswestry and Roland-Morris Disability Questionnaires. *Clin Orthop Relat Res* 2003; 411:40–53.
10. Bush K, Hillier S. A controlled study of caudal epidural injections of triamcinolone plus procaine for the management of intractable sciatica. *Spine* 1991;16:572–5.
11. Cuckler JM, Bernini PA, Wiesel SW, et al. The use of epidural steroids in the treatment of lumbar radicular pain: a prospective, randomized, double blind study. *J Bone Joint Surg Am* 1985;67:63–6.
12. Singh V, Manchikanti L. Role of caudal epidural injections in the management of chronic low back pain. *Pain Physician* 2002;5:133–48.
13. Ogoke BA. Caudal epidural steroid injections. *Pain Physician* 2000;3:305–12.
14. Dashfield AK, Taylor MB, Cleaver JS, et al. Comparison of caudal epidural with targeted steroid placement during spinal endoscopy for chronic sciatica: a prospective randomised double-blind trial. *Br J Anesth* 2005;94:514–9.
15. Hayashi N, Weinstein JN, Meller ST, et al. The effect of epidural injection of betamethasone or bupivacaine in a rat model of lumbar radiculopathy. *Spine* 1998;23:877–85.
16. Marshall LL, Trethewie EW, Curtain CC. Chemical irritation of nerve-root in disc prolapse. *Lancet* 1973;2:320.
17. Marshall LL, Trethewie EW, Curtain CC. Chemical radiculitis: a clinical, physiological, and immunological study. *Clin Orthop* 1977;129:61–7.

18. Saal JS, Franson RC, Dobrow R, et al. High levels of inflammatory phospholipase A2 activity in lumbar disc herniations. *Spine* 1990;15:674–8.
19. Kayama S, Konno S, Olmarker K, et al. Incision of the annulus fibrosus induces nerve root morphologic, vascular, and functional changes. *Spine* 1996;21:2539–43.
20. Chaoyang C, Cavanaugh JM, Ozaktaky C, et al. Effects of phospholipase A2 on lumbar nerve root structure and function. *Spine* 1997;22:1057–64.
21. Olmarker K, Blomquist J, Stromberg J, et al. Inflammatogenic properties of nucleus pulposus. *Spine* 1995;20:665–9.
22. Kang JD, Georgescu HI, McIntyre-Larkin L, et al. Herniated lumbar intervertebral discs spontaneously produce matrix metalloproteinases, nitric oxide, interleukin-6, and prostaglandin E2. *Spine* 1996;21:271–7.
23. Olmarker K, Rydevik B, Nordborg C. Autologous nucleus pulposus induces neurophysiologic and histologic changes in porcine cauda equina nerve roots. *Spine* 1993;18:1425–32.
24. Grönblad M, Virri J, Tolonen J, et al. A controlled immunohistochemical study of inflammatory cells in disc herniation tissue. *Spine* 1994;19:2744–51.
25. Kawakami M, Tamaki T, Hashizume H, et al. The role of phospholipase A2 and nitric oxide in pain-related behavior produced by an allograft of intervertebral disc material to the sciatic nerve of the rat. *Spine* 1997;22:1074–9.
26. Saal JS. The role of inflammation in lumbar pain. *Spine* 1995;20:1821–7.
27. Thelander U, Fagerlund M, Friberg S, et al. Straight leg raising test *versus* radiologic size, shape, and position of lumbar disc herniations. *Spine* 1992;17:395–9.
28. Haldeman S. North American Spine Society: failure of the pathology model to predict back pain. *Spine* 1990;15:718–32.
29. Olmarker K, Byrod G, Cornefijord M, et al. Effects of methylprednisolone on nucleus pulposus-induced nerve root injury. *Spine* 1994;19:1803–8.
30. Minamide A, Tamaki T, Hashizume H, et al. Effects of steroid and lipopolysaccharide on spontaneous resorption of herniated intervertebral discs: an experience study in the rabbit. *Spine* 1998;23:870–6.
31. Weinstein JN, Tosteson TD, Lurie JD, et al. Surgical vs. nonoperative treatment for lumbar disc herniation: the Spine Patient Outcomes Research Trial (SPORT): a randomized trial. *JAMA* 2006;296:2441–50.
32. Atlas SJ, Keller RB, Wu YA, et al. Long-term outcomes of surgical and nonsurgical management of sciatica secondary to a lumbar disc herniation: 10 year results from the maine lumbar spine study. *Spine* 2005;30:927–35.
33. Renfrew DL, Moore TE, Kathol MH, et al. Correct placement of epidural steroid injections: fluoroscopic guidance and contrast administration. *Am J Neuroradiol* 1991;12:1003–7.
34. Eastwood D, Williams C, Buchan I. Caudal epidurals: the whoosh test. *Anaesthesia* 1998;53:305–7.
35. Tsui BC, Tarkkila P, Gupta S, et al. Confirmation of caudal needle placement using nerve stimulation. *Anesthesiology* 1999;91:374–8.
36. Stitz MY, Sommer HM. Accuracy of blind *versus* fluoroscopically guided caudal epidural injection. *Spine* 1999;24:1371–6.