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RANDOMIZED TRIAL

Transforaminal Epidural Clonidine *Versus* Corticosteroid for Acute Lumbosacral Radiculopathy due to Intervertebral Disc Herniation

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Study Design. Randomized, double-blinded clinical trial.

Objective. To compare efficacies of two active therapies for chronic low back pain.

Summary of Background Data. Radicular pain may result from intervertebral disc herniation. Clonidine has demonstrated analgesic and anti-inflammatory activity in animal studies on nerve injury. Extensive clinical experience supports neuraxial clonidine's safety.

Methods. Patients with approximately 3 months of low back pain and leg pain due to intervertebral disc herniation were randomized to transforaminal epidural injection(s) of 2% lidocaine and either clonidine (200 or 400 μg) or triamcinolone (40 mg). Patients received one to three injections administered at about 2 weeks apart. Patients, investigators, and study coordinators were blinded to the treatment. The primary outcome was an 11-point Pain Intensity Numerical Rating Scale at 1 month. Other outcomes included Patient Global Impression of Change and functional measures.

Results. Of the 33 patients screened and randomized, 26 enrolled, of which 11 received clonidine and 15 triamcinolone. Both groups showed significant improvement in pain score at 2 weeks and 1 month compared with baseline ($P < 0.05$). The corticosteroid group showed additional functional improvement at 1 month with respect to clonidine ($P = 0.022$). There was no difference between groups for primary outcome. However, as target enrollment was not reached, we cannot say with confidence that the two treatments would be expected to result in similar short-term pain relief. Adverse effects were common in both groups, but there were no serious complications.

Conclusions. Radicular pain due to intervertebral disc herniation improved rapidly with transforaminal epidural injection of either clonidine or triamcinolone. Corticosteroid resulted in greater functional improvement, with unclear differences in analgesia. Future studies will determine whether clonidine is superior to placebo and is of particular use in those at risk for corticosteroid complications.

Key words: Intervertebral disc hernation, radiculopathy, clonidine, epidural injection, corticosteroid, pain. **Spine 2011;36:E293–E300**

Intervertebral disc herniation (IDH) leading to radiculopathy is a common clinical problem in Western countries.[1] Pain and other neurologic symptoms associated with this condition are likely a result of mechanical compression and local inflammation of spinal nerve roots.[2] Treatment methods include oral pain medications, physical therapy, epidural steroid injection (ESI), and surgery, among others. Both ESI and surgery appear to result in short-term pain relief relative to more conservative measures, yet neither is clearly superior to the other in observation at 1-year follow-up.[3,4] Moreover, corticosteroid administration is limited by systemic toxicity and rare but serious complications, while surgery is only moderately cost-effective and requires hospitalization and postoperative recuperation.[5,6]

Clonidine, originally developed as an antihypertensive, is approved by the US Food and Drug Administration for epidural administration in the treatment of cancer pain (http://www.accessdata.fda.gov/Scripts/cder/DrugsatFDA/index.cfm?fuseaction=Search.Label_ApprovalHistory#apphist). Multiple animal and human studies as well as clinical experience support the safety and potential efficacy of both neuraxial and perineural administration of clonidine.[7–9] In addition to

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analgesia mediated by its action at $\acute{\alpha}_2$-adrenergic receptors located in the central and peripheral nervous system, clonidine may have anti-inflammatory activity that could influence pain by other mechanisms.[7,10,11] In animal models, administration of clonidine at the site of mechanical or chemical nerve injury decreased hyperalgesia, modulated local cytokine expression, and mitigated histologic changes seen with nerve injury.[10,12–14]

Clonidine's safety record and dual action as an analgesic and anti-inflammatory agent in the setting of peripheral nerve injury make it an intriguing alternative to ESI for radicular pain. We hypothesized that clonidine administered in close proximity to the site of nerve injury in patients with spinal nerve–root displacement due to IDH would result in greater improvement in pain relative to corticosteroid. We investigated this hypothesis by comparing serial transforaminal epidural (TFE) injection of clonidine with triamcinolone, using a randomized, double-blinded study design.

MATERIALS AND METHODS

We conducted a single-center, prospective study evaluating patients with 3 or less months of low back pain and leg pain due to IDH. The medical ethics committee for investigation of human subjects approved the study protocol before opening enrollment and the trial was registered at the Web site: www.clinicaltrials.gov (NCT00588354). All patients provided written informed consent before study inclusion.

Patients

Eligible patients were 18 years or older, of either sex, and local residents. Enrollment opened in November 2006 and closed in November 2008. Patients were evaluated at a multidisciplinary spine center or pain clinic at our institution where they were given a diagnosis of IDH with resultant low back pain and leg pain due to encroachment of disc material on a spinal nerve-root as confirmed by computed tomography or magnetic resonance imaging. All patients had a positive nerve-root tension sign on physical examination with unilateral symptoms at a single level of the lumbosacral spine, consistent with magnetic resonance imaging findings.

Pain intensity was assessed for each patient using a Pain Intensity Numerical Rating Scale (PI-NRS) from 0 to 10 (0 is no pain and 10 is worst pain imaginable). Patients were excluded if pain was less than 3 of 10 or more than 8 of 10 if already taking opioids. Additional exclusion criteria were as follows: history of recent spinal trauma; cauda equina syndrome; progressive motor deficit; chronic anticoagulation other than aspirin; infectious etiology; involvement in workers' compensation claim; history of adverse reaction to corticosteroids, local anesthetic, or clonidine; history of one or more corticosteroid injection (equivalent to 40 mg or more of triamcinolone) in the preceding 4 months; pregnancy; or severe medical disease (*e.g.*, uncontrolled diabetes mellitus or coronary artery disease).

Randomization, Blinding, and Treatment

Using a block randomization scheme applied to all patients screened, patients were assigned to one group receiving transforaminal ESI with local anesthetic (40- or 80-mg triamcinolone diluted to 2-mL total volume with preservative-free normal saline, preceded by a test dose of 1-mL 2% lidocaine) or another receiving TFE clonidine with local anesthetic (200- or 400-μg clonidine diluted to 2-mL total volume with preservative-free normal saline, preceded by a test dose of 1-mL 2% lidocaine). Those in the clonidine group were administered a lower dose at first injection and, if tolerated, received a higher dose at subsequent injections. Patients, investigators, and all others with direct patient contact were blinded to treatment assignment. Only the research pharmacy at our institution knew the treatment assignment. A syringe containing the study drug (triamcinolone or clonidine) was provided by the pharmacy at each injection visit, but contents of the syringe were masked. Patients were offered up to three injections and asked to commit to at least one. The first injection was given on the day of enrollment and further injections were given at 10- to 14-day intervals. Injections were administered using fluoroscopic guidance and a transforaminal retroneural approach as described in the International Spine Intervention Society Practice Guidelines, 2004.[15] Figures 1 and 2 are radiographs that demonstrate the technique. An institutional protocol including contrast-enhanced digital subtraction angiography was used to minimize the risk of intravascular needle placement and confirm injectate spread along the nerve root and into the epidural space at the target level. Before discharge, patients were monitored in a postprocedure setting for at least 60 minutes after injection.

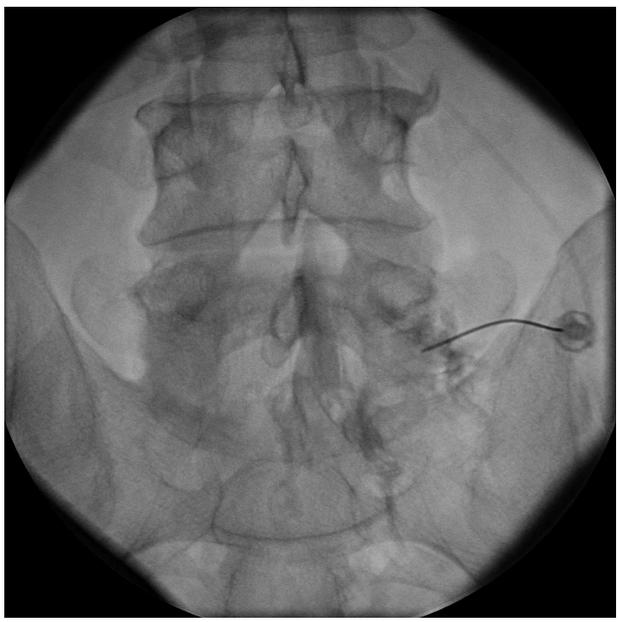

Figure 1. Anteroposterior radiographic view of needle in final position within the target neuroforamen. Radiographic contrast is seen along the nerve root and in the epidural space at the target vertebral segment.

Injections and other care, dictated by study protocol, were administered by a board-certified pain management physician. Saved radiographic images from injections were reviewed by two of the investigators (A.H.B. and M.A.H.) before breaking the blind to verify correct needle placement. Patients were provided prescriptions or referrals for oral anti-inflammatories,

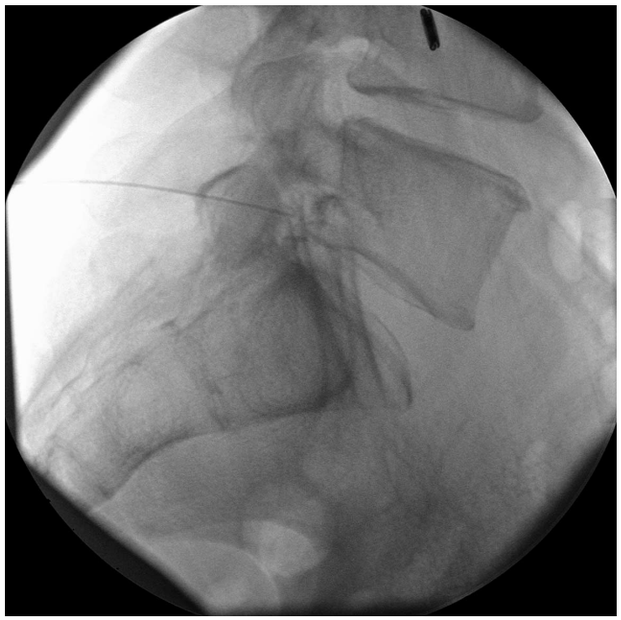

Figure 2. Lateral radiographic view of needle in final position within the target neuroforamen. Radiographic contrast is seen in the anterior epidural space, in close proximity to the putative site of nerve injury.

oral anticonvulsant or antidepressant pain medications, oral opioid analgesics, physical therapy, or more intensive medical or surgical therapy as indicated. Those experiencing worsening of pain as rated on the 0 to 10 PI-NRS at 1 month were offered rescue therapy, an unblinded, fluoroscopically guided transforaminal or interlaminar epidural injection containing 40- to 80-mg triamcinolone. A patient flowchart is shown (Figure 3).

Study Measures

Primary outcome measure was an 11-point PI-NRS at 1 month after enrollment. Other outcome measures were 7-point Patient Global Impression of Change, Multidimensional Pain Inventory, Center for Epidemiologic Studies Depression Scale, Roland-Morris Disability Questionnaire (RMDQ), and Oswestry Disability Index (ODI). Measures were examined at enrollment, immediately prior to second injection (or 10–14 days after enrollment if only one injection was administered) and immediately prior to third injection (or 20–28 days after enrollment if fewer than three injections were administered). Adverse effects as reported by patients were recorded in an unedited format. Occurrence of surgery for the index pain generator was evaluated for up to 6 months after enrollment.

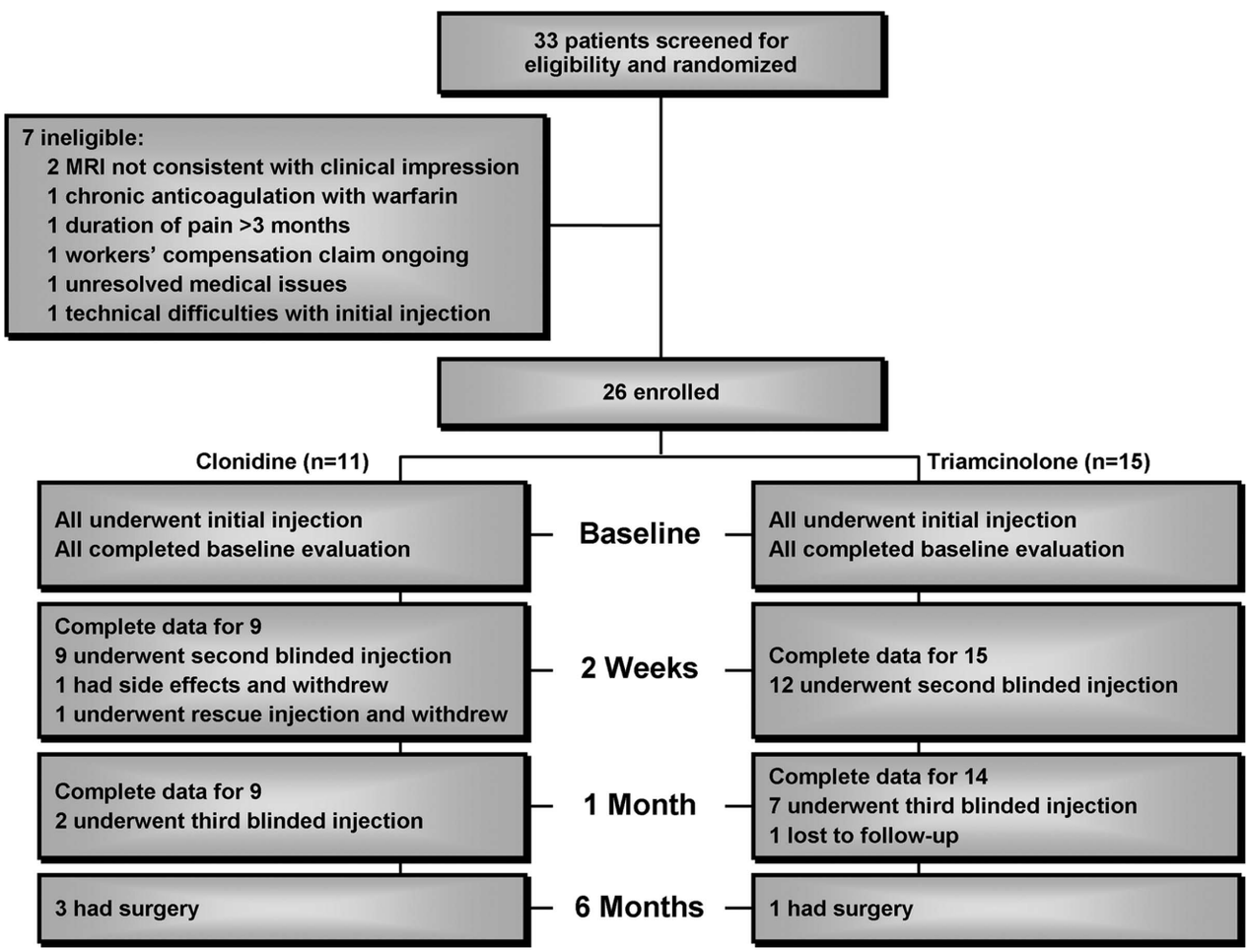

Figure 3. Patient flowchart demonstrating enrollment, randomization, and follow-up periods.

Statistical Analysis

Baseline characteristics were compared between groups by using the wilcoxon rank sum test for continuous variables and an exact test for categorical variables. Treatment comparisons of the outcome variables were performed using analysis of covariance with treatment (clonidine *vs*. steroid) as the independent variable and the baseline value included as a covariate. Within each treatment group, postrandomization measurements were compared with baseline using the paired *t* test. The frequency of adverse effects and other binomial outcomes were compared between treatment groups by using Fisher exact test. In all cases, 2-tailed $P \leq 0.05$ were considered statistically significant.

On the basis of data from two clinical trials of patients with radiculopathy, we determined that a sample size of 20 patients in each group would provide statistical power (2-tailed, $\alpha = .05$) to detect a difference of 2 points on the 11-point PI-NRS,[16,17] allowing for dropout of up to 15%. However, because of slow recruitment, a decision was made to discontinue enrollment after 26 patients had been enrolled. The decision to discontinue enrollment was made before breaking the blind or performing any data analysis. Given the reduced sample size, treatment effects (clonidine *vs*. steroid) are summarized using point estimates and corresponding 95% confidence intervals (CI).

RESULTS

Baseline patient characteristics were similar between treatment groups (Table 1). Analyses of outcomes at 2 weeks and 4 weeks after randomization are summarized in Table 2. For each treatment group there was evidence of a significant (paired *t* test, $P < 0.05$) improvement from baseline for PI-NRS at both 2 weeks and 4 weeks after randomization (Figure 4). However, for the primary endpoint of PI-NRS at 4 weeks after randomization, there was no significant difference between treatment groups (clonidine *vs*. steroid treatment effect = +1.54, 95% CI = −0.52 to +3.60; $P = 0.159$). For the secondary endpoints of RMDQ and ODI, there was evidence of a significant improvement from baseline at both 2 weeks and 4 weeks after randomization for the steroid group. For the clonidine group, these secondary endpoints tended to improve, but the changes from baseline were not statistically significant (paired *t* test, $P = 0.062$ and $P = 0.091$ for RMDQ at 2 weeks and 4 weeks, respectively; $P = 0.171$ and $P = 0.076$ for ODI at 2 weeks and 4 weeks, respectively). At 4 weeks after randomization, significant treatment effects were detected for RMDQ (clonidine *vs*. steroid treatment effect = +5.67, 95% CI = +1.22 to +10.12; $P = 0.022$ [Figure 2]) and ODI (clonidine *vs*. steroid treatment effect = +7.04, 95% CI = +0.83 to +13.25; $P = 0.038$). Results for RMDQ are shown in Figure 5. Multidimensional Pain Inventory did not differ significantly from baseline at 2 weeks or 4 weeks for either treatment group (paired *t* test, all $P > 0.05$).

Sixty-seven percent of patients allocated to receive clonidine and 50% of those administered corticosteroid rated their course as "much improved" (Patient Global Impression of Change ≤ 2) at 1 month, a difference that was not significant (Fisher exact test, $P = 0.669$). Patients were allowed to receive up to three injections, a decision that depended on both patient desire and clinician recommendation. There were 22 and 34 total injections in the clonidine and corticosteroid groups, respectively. Two of the 11 (18%) clonidine patients

TABLE 1. Baseline Patient Characteristics

Characteristic	Clonidine (n = 11)	Steroid (n= 15)	*P**
Age, yr			0.161
Mean (SD)	44.1 (12.4)	50.3 (11.0)	
Median (range)	40 (28–72)	49 (33–71)	
Gender			0.658
Male	9 (82)	10 (67)	
Female	2 (18)	5 (33)	
Level injected, n (%)			0.865
L3	0 (0)	1 (7)	
L4	2 (18)	4 (27)	
L5	4 (36)	3 (20)	
S1	5 (45)	7 (47)	
Use of opioids, n (%)	10 (91)	10 (67)	0.197
Use of antiepileptics, n (%)	5 (45)	4 (27)	0.418
Duration of symptoms, wk			0.649
Mean (SD)	5.0 (2.5)	5.3 (3.7)	
Median (range)	4 (3–12)	4 (1–12)	
PI-NRS			0.751
Mean (SD)	7.0 (1.9)	7.0 (2.0)	
Median (range)	7 (3–9)	7 (3–10)	
RMDQ			0.124
Mean (SD)	14.0 (3.8)	11.0 (5.2)	
Median (range)	16 (7–19)	11 (3–19)	
ODI			0.153
Mean (SD)	31.3 (6.0)	28.8 (7.2)	
Median (range)	33 (18–37)	27 (21–48)	
MPI			0.378
Mean (SD)	56.9 (12.7)	52.9 (9.1)	
Median (range)	57.4 (37.7–74.1)	54.8 (29.1–65.6)	
CESD			0.979
Mean (SD)	15.2 (13.0)	12.5 (7.7)	
Median (range)	11 (1–36)	14 (3–26)	

**Rank sum test for continuous variables, Fisher exact test for categorical variables.*

CESD indicates Center for Epidemiologic Studies Depression Scale; MPI, Multidimensional Pain Inventory; ODI, Oswestry Disability Index; PI-NRS, Pain Intensity Numerical Rating Scale; RMDQ, Roland-Morris Disability Questionnaire; and SD, standard deviation.

TABLE 2. Treatment Effects at 2 and 4 Weeks After Randomization*

	Estimate	SE	95% CI	*P*
Wk 2				
PI-NRS	0.11	0.97	−1.79, 2.01	0.910
RMDQ	2.96	2.04	−1.04, 6.96	0.162
ODI	5.86	3.28	−0.57, 12.29	0.089
MPI	−4.83	3.53	−11.75, 2.09	0.186
Wk 4				
PI-NRS	1.54	1.05	−0.52, 3.60	0.159
RMDQ	5.67	2.27	1.22, 10.12	0.022
ODI	7.04	3.17	0.83, 13.25	0.038
MPI	−0.35	3.37	−6.96, 6.26	0.918

**Data were analyzed separately for each measure using analysis of covariance with treatment (clonidine vs. steroid) as the independent variable and the baseline value of the given measure included as a covariate. At 2 weeks, data were available for 24 patients (9 clonidine and 15 steroid) and at 4 weeks, data were available for 23 patients (9 clonidine and 14 steroid).*

CI indicates confidence interval; MPI, Multidimensional Pain Inventory; ODI, Oswestry Disability Index; PI-NRS, Pain Intensity Numerical Rating Scale; RMDQ, Roland-Morris Disability Questionnaire; and SE, standard error.

were administered all three injections, while 7 of the 15 (47%) corticosteroid patients received three injections (Fisher exact test, $P = 0.217$). At 6 months, three patients receiving clonidine and one patient receiving triamcinolone had undergone lumbar spine surgery (Fisher exact test, $P = 0.279$). Adverse effects were common, but none were serious and no patient required postinjection hospitalization due to adverse effects (Table 3).

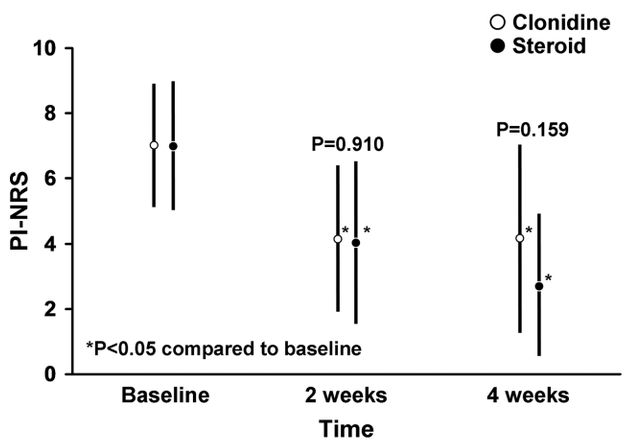

Figure 4. Mean (±SD) pain intensity numeric rating scale according to treatment group at baseline and also at 2 weeks and 4 weeks after randomization. The *P* values presented for the 2-week and 4-week postrandomization time periods correspond to the treatment effect from analysis of covariance with treatment (clonidine *vs.* steroid) as the independent variable and the baseline value included as a covariate. For each treatment group, a "*" is used to denote significant differences from baseline (paired *t* test $P < 0.05$).

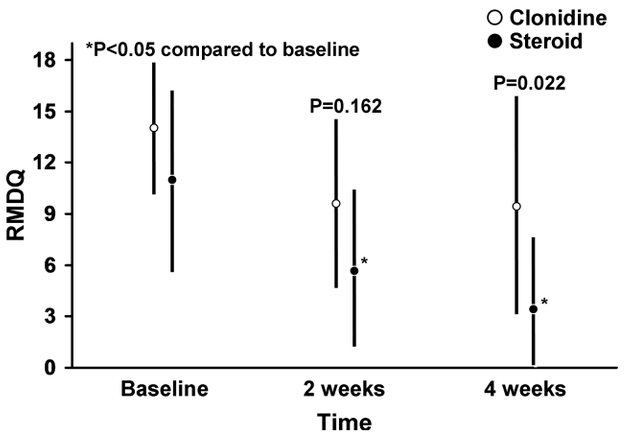

Figure 5. Mean (±SD) Roland Morris Disability Questionnaire according to treatment group at baseline and also at 2 weeks and 4 weeks after randomization. The *P* values presented for the 2-week and 4-week postrandomization time periods correspond to the treatment effect from analysis of covariance with treatment (clonidine *vs.* steroid) as the independent variable and the baseline value included as a covariate. For each treatment group, a "*" is used to denote significant differences from baseline (paired *t* test $P < 0.05$).

DISCUSSION

This is the first clinical trial to examine TFE clonidine *versus* a similar injection of corticosteroid for the treatment of acute radicular pain due to IDH. Consistent with other clinical trials of epidural injection for lumbosacral radicular pain, patients in both groups showed short-term improvement after enrollment, with the corticosteroid group demonstrating additional functional improvement relative to clonidine at 1 month. To our knowledge, no previous randomized, blinded study has shown functional improvement with ESI relative to comparator treatment. We did not reach target enrollment as determined by a prestudy power analysis for the primary outcome PI-NRS at 1 month. As such, although we did not find a statistically

TABLE 3. Adverse Effects*

Adverse Effects	Clonidine (n = 11)	Steroid (n = 15)
Discomfort at injection site	2 (18)	4 (27)
Worsening of symptoms	4 (36)	2 (13)
Lightheadedness	5 (45)	1 (7)
Drowsiness	2 (18)	3 (20)
Dry mouth	2 (18)	3 (20)
Weakness	4 (36)	1 (7)
Constipation	2 (18)	1 (7)
Nausea	1 (9)	2 (13)

**No patient required hospitalization for adverse effects. However, one patient in the clonidine group reported nausea and lightheadedness and discontinued study participation because of these adverse effects. The frequency of each adverse effect was compared between groups using Fisher exact test with no significant ($P < 0.05$) differences detected.*

significant difference in pain relief between the two study arms, we cannot say with confidence that no difference exists.

Rationale

Radiculopathy associated with disc herniation is hypothesized to occur by two independent mechanisms: mechanical compression and cytokine-mediated radiculitis.[2] Tumor necrosis factor-alpha may be the cytokine of primary importance in the pathophysiology relating to the latter.[18,19] Recently, Cohen *et al*[20] completed a randomized, blinded trial, in which 18 patients received TFE injection of the tumor necrosis factor-alpha inhibitor, etanercept, for subacute to chronic lumbosacral radiculopathy because of IDH.[20] At 1 month, primary outcome pain scores were lower in the etanercept participants than in a small placebo group.

Clonidine is an attractive potential alternative therapy for IDH because it appears to be both analgesic and anti-inflammatory, is not expected to be associated with cumulative dose toxicity, and has a long clinical track record of safety. Furthermore, since clonidine is a nonparticulate solution prior to injection, it may not carry the same risks of central nervous system infarction that have been attributed to particulate steroids injected *via* the TFE route.[21,22] Clonidine's direct analgesic effect is primarily mediated through agonism at $\acute{\alpha}_2$-adrenergic receptors, which can be found on peripheral nerves and in the spinal cord and brainstem. Anti-inflammatory effects of clonidine have been noted in a number of preclinical studies of nerve injury and may also indirectly influence pain.[10,12–14] Clonidine reduced tissue content of cytokines, including tumor necrosis factor-alpha, in rats undergoing sciatic nerve ligation, particularly with serial administration.[10] Other possible mechanisms for analgesia produced by clonidine, as administered in our study, exist, including blockade of C and A-δ fibers, increased potassium conductance, and augmentation of local anesthetic block.[7]

Outcomes

Patients in our study demonstrated statistically and clinically significant improvements in pain score at both 2 weeks and 1 month after enrollment, regardless of group assignment.[23,24] There were no significant differences between the study arms with regard to PI-NRS, Patient Global Impression of Change, Multidimensional Pain Inventory, Center for Epidemiologic Studies Depression Scale, number of injections, or rate of surgery. However, patients in the corticosteroid group did show statistically significant functional improvement (as measured on RMDQ and ODI) with respect to clonidine at 1 month.[24] The reason why the corticosteroid group exhibited functional improvement, but no difference in other outcome measures relative to clonidine, is not clear. The simplest explanation could be that triamcinolone is superior to clonidine for IDH, and that if our study were larger, and therefore appropriately powered, a statistically-significant difference in pain relief would have emerged. Other potential explanations exist, including that the pain rating, global change, and pain interference measurement tools we used were not as sensitive as our functional measures, or that clonidine's different pharmacodynamic profile results in an alternate mechanism leading to similar pain relief. For instance, clonidine may have weaker anti-inflammatory activity than corticosteroid but with a stronger analgesic effect.

Carette *et al*[16] randomized patients with radicular pain due to IDH for less than 1 year to interlaminar epidural injection of methylprednisolone or saline. Pain scores on a 100-point visual analog scale fell an average of 21 and 12 points, respectively, 3 weeks after enrollment.[16] We saw a mean decline of 2.9 and 4.6 points (on an 11-point scale) in the clonidine and triamcinolone groups, respectively, at 1 month, a difference suggestive of greater treatment effect in both of our groups relative to either group in Carette *et al*.[16] ODI showed a greater mean reduction at 1 month in patients receiving triamcinolone (but not clonidine) in our study compared with either group in Carette *et al*[16] at 3 weeks. If these apparent differences are real, they could be due to a variety of factors, including different access routes to the epidural space (interlaminar epidural space in Carette *et al*[16] *vs*. TFE in our study), differences in symptom duration (longer in Carette *et al*[16]), or simply different outcome intervals. Rates of surgery vary widely among patients with lumbosacral radiculopathy, ranging from 15% to almost 45% at follow-up up to 2 years.[16,17,25,26] We recorded occurrence of surgery at 6 months among all patients enrolled and found an overall incidence of 4 of 26 (15%), with no difference between the study arms.

Adverse effects were noted in both study groups but no serious complications occurred and no patient required hospital admission after injection. An escalating dosage schedule of clonidine was used so that any patient who noted clonidine-specific, but not serious, adverse effects could remain in the study and continue to receive a relatively low clonidine dose. However, all patients who had more than 1 clonidine injection were administered the higher dose at subsequent injections. Interestingly, the complication we thought most likely in the clonidine group—hypotension—was observed in a single patient who was in the corticosteroid arm. This patient was nonsymptomatic and the hypotension was resolved with fluid and extended stay in the outpatient area. One patient in the clonidine group withdrew from the study because of adverse effects. This patient listed nausea and lightheadedness as the reason for withdrawal but did not decide to withdraw from the study until the 2-week follow-up visit. Overall, we had no indication that clonidine could not be safely administered in the outpatient setting using our dosage regimen.

Limitations

This study had a number of limitations. First, our hypothesis was that there would be a difference in the two study arms in pain score at 1 month after enrollment. We did not find a difference, but since we failed to reach target enrollment, we cannot say with confidence that the study groups were similar with respect to primary outcome. We chose not to perform a *post hoc* power analysis. Our small sample size was also likely the cause of unequal distribution of participants, with more patients assigned to receive corticosteroid than clonidine.

Unfortunately, more screened patients who had been allocated to clonidine were deemed ineligible prior to enrollment.

Second, we chose clonidine because of its potential dual mechanism as an analgesic and anti-inflammatory. However, we did not measure analgesia during the expected analgesic peak of bolus epidural administration. Instead, we collected data 10 or more days after the last injection. Perhaps prolonged residence time at the site of nerve injury (*e.g.*, continuous infusion, depot drug) or more frequent injection would have enhanced clonidine's effect.[7] Currently, however, technological and cost limitations preclude more frequent or continuous administration of clonidine for the condition under study.

Third, we compared clonidine with an active control, rather than with placebo. We cannot, therefore, comment on the efficacy relative to sham of either TFE clonidine or corticosteroid administered using our study protocol. Since the natural history of IDH is rapid improvement, results in either group cannot be stated to differ from those expected without interventional treatment among patients enrolled.[3,27] However, we chose our study design to provide practical evidence reflecting a subset of decisions clinicians must face (corticosteroid injection *vs*. novel therapy). In addition, we thought it unfair to withhold active treatment since there is evidence of short-term symptomatic improvement with corticosteroid among patients similar to those enrolled in our trial.[4]

SUMMARY

Patients with acute radicular pain due to IDH demonstrated short-term improvement using a treatment approach, which included either TFE corticosteroid or clonidine. There was no difference in pain score between the two study groups, a finding that could be at least partly due to the small number of patients enrolled. Clonidine administration resulted in no major adverse events, indicating that despite inferiority in our study, its risk-benefit profile may still be superior to corticosteroid in special populations at risk for corticosteroid-associated complications. Future studies should (1) compare clonidine to placebo, (2) consider additional outcome measures, (3) examine alternate dosage and injection intervals for clonidine, and (4) include special populations at risk for steroid-associated complications.

➢ Key Points

- ❑ Patients with acute lumbosacral radicular pain due to intervertebral disc herniation improve rapidly with a treatment approach that includes serial transforaminal epidural injections.
- ❑ Transforaminal epidural injection of triamcinolone results in greater improvement relative to clonidine on two commonly used functional measures for low back pain.
- ❑ Pain relief with triamcinolone is not clearly superior to clonidine, although the current study was not adequately powered to assess this outcome.
- ❑ Despite apparent inferiority in this study, clonidine may still be an attractive alternative to corticosteroid for patients with intervertebral disc herniation who are at risk for corticosteroid-associated complications.

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