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Oral Steroids for Acute Radiculopathy Due to a Herniated Lumbar Disk:

A Randomized Clinical Trial

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Abstract

IMPORTANCE—Oral steroids are commonly used to treat acute sciatica due to a herniated disk but have not been evaluated in an appropriately powered clinical trial.

OBJECTIVE—To determine if oral prednisone is more effective than placebo in improving function and pain among patients with acute sciatica.

DESIGN, SETTING, AND PARTICIPANTS—Randomized, double-blind, placebo-controlled clinical trial conducted from 2008 to 2013 in a large integrated health care delivery system in Northern California. Adults (n=269) with radicular pain for 3 months or less, an Oswestry Disability Index (ODI) score of 30 or higher (range, 0-100; higher scores indicate greater dysfunction), and a herniated disk confirmed by magnetic resonance imaging were eligible.

INTERVENTIONS—Participants were randomly assigned in a 2:1 ratio to receive a tapering 15-day course of oral prednisone (5 days each of 60mg, 40mg, and 20mg; total cumulative dose = 600mg; n = 181) or matching placebo (n = 88).

MAIN OUTCOMES AND MEASURES—The primary outcome was ODI change at 3 weeks; secondary outcomes were ODI change at 1 year, change in lower extremity pain (measured on a 0-10 scale; higher scores indicate more pain), spine surgery, and Short Form 36 Health Survey (SF-36) Physical Component Summary (PCS) and Mental Component Summary (MCS) scores (0-100 scale; higher scores better).

RESULTS—Observed baseline and 3-week mean ODI scores were 51.2 and 32.2 for the prednisone group and 51.1 and 37.5 for the placebo group, respectively. The prednisone-treated group showed an adjusted mean 6.4-point (95%CI, 1.9-10.9; $P = .006$) greater improvement in ODI scores at 3 weeks than the placebo group and a mean 7.4-point (95%CI, 2.2-12.5; $P = .005$) greater improvement at 52 weeks. Compared with the placebo group, the prednisone group showed an adjusted mean 0.3-point (95%CI, −0.4 to 1.0; $P = .34$) greater reduction in pain at 3 weeks and a mean 0.6-point (95%CI, −0.2 to 1.3; $P = .15$) greater reduction at 52 weeks. The prednisone group showed an adjusted mean 3.3-point (95%CI, 1.3-5.2; $P = .001$) greater

improvement in the SF-36 PCS score at 3 weeks, no difference in the SF-36 PCS score at 52 weeks (mean, 2.5; 95%CI, −0.3 to 5.4; $P = .08$), no change in the SF-36MCS score at 3 weeks (mean, 2.2; 95%CI, −0.4 to 4.8; $P = .10$), and an adjusted 3.6-point (95%CI, 0.6-6.7; $P = .02$) greater improvement in the SF-36MCS score at 52 weeks. There were no differences in surgery rates at 52-week follow-up. Having 1 or more adverse events at 3-week follow-up was more common in the prednisone group than in the placebo group (49.2% vs 23.9%; $P < .001$).

CONCLUSIONS AND RELEVANCE—Among patients with acute radiculopathy due to a herniated lumbar disk, a short course of oral steroids, compared with placebo, resulted in modestly improved function and no improvement in pain.

TRIAL REGISTRATION—clinicaltrials.gov Identifier: NCT00668434

Acute lumbar radiculopathy (sciatica) is characterized by radiating buttock and leg pain in a lumbar nerve root distribution.[1,2] It is commonly associated with the herniation of the nucleus pulposus[3,4] and has a lifetime prevalence exceeding 10%.[5] Spontaneous recovery occurs in most patients; however, many endure substantial pain and disability.[2,3,6] For those who do not recover quickly, invasive procedures such as epidural steroid injections (ESIs) and lumbar diskectomy are commonly performed.[3,7,8] Accelerating the process of recovery would provide substantial benefits to affected patients and potentially reduce the need for expensive invasive procedures.

Despite conflicting evidence, ESIs are frequently offered under the assumption that radicular symptoms are caused by inflammation of the affected lumbar nerve root.[4,9-11] Epidural steroid injections are invasive, generally require a preprocedure magnetic resonance imaging (MRI) study, and expose patients to fluoroscopic radiation. In addition, the US Food and Drug Administration recently warned of rare but serious neurologic sequelae from ESIs.[12,13] Oral administration of steroid medication may provide similar anti-inflammatory activity, does not require an MRI or radiation exposure, can be delivered quickly by primary care physicians, carries less risk, and would be much less expensive than an ESI. Oral steroids are used by many community physicians, have been included in some clinical guidelines,[14] and are noted as a treatment option by some authors.[15,16] However, no appropriately powered clinical trials of oral steroids for radiculopathy have been conducted to date.[17]

To address this issue, we performed a parallel-group, double-blind randomized clinical trial of a 15-day tapering course of oral prednisone vs placebo for patients with an acute lumbar radiculopathy associated with a herniated lumbar disk. The trial protocol is available in the Supplement.

Methods

Participants

Eligible patients (Figure 1) were members of Kaiser Permanente Northern California, were aged 18 to 70 years, reported leg pain extending below the knee in a nerve root distribution, had a herniated disk confirmed by MRI, and scored 30 points or higher on the Oswestry Disability Index[18] (ODI; this cut point was chosen from a pilot study as the approximate median ODI score among similar patients). Exclusion criteria included onset of radicular

pain more than 3 months prior, previous lumbar surgery, oral or epidural steroid treatment in the prior 3 months, diabetes, substantial or progressive motor loss, and/or ongoing litigation or workers compensation claim. A positive straight-leg raise test result was initially an inclusion criterion that was eliminated after 14 months to improve recruitment and allow interaction analyses with this characteristic. Participants were recruited from primary care practices at 3 Kaiser Permanente Northern California facilities and from a daily extract of the electronic medical record. Race/ethnicity data were self-reported. (This National Institutes of Health–funded study was required to collect and annually report data on race and ethnicity for all participants. We used these data in preplanned subgroup analyses examining potential interaction with demographic variables; see section 2.3 of the trial protocol in the Supplement.)

Intervention

Participants randomized to the active treatment group took three 20-mg capsules of prednisone daily for 5 days, then 2 capsules daily for 5 days, then 1 capsule daily for 5 days (this cumulative dose of 600 mg was thought to provide sufficient antiinflammatory effect and was in common use in local practice). Participants in the placebo group received identical-appearing capsules and instructions. Nonsteroidal anti-inflammatory drugs were not allowed for 3 weeks after randomization, but otherwise all patients in both treatment groups received usual care for their symptoms.

Outcomes

The primary outcome was self-reported score on the ODI, version 2.0 (measured on a 0- to 100-point scale, with higher scores indicating greater dysfunction)[18] measured 3 weeks after randomization. We chose this time point for the primary outcome because we were most interested in testing whether oral steroids could more rapidly return patients to higher functioning and less pain in the early, more symptomatic weeks of an acute sciatica episode. Predefined secondary outcomes were a pain numerical rating scale (NRS) scored on a 0- to 10-point scale (higher numbers indicating more pain) that inquired about participants' average, best, and worst levels of pain below the waist over the prior 3 days and participants' average pain levels above the waist, the Short Form 36 Health Survey Physical Component Summary and Mental Component Summary subscale scores (each measured on 0- to 100-point scales, with higher scores indicating better health status),[19] and incidence of lumbar spine surgery. An additional measure assessed participants' global assessment of improvement by asking participants to rate how much their leg pain had changed since taking the study medication (measured on a Likert scale from 1 [very much better] to 7 [very much worse]).

Study Procedures

After providing informed consent, patients were reviewed for eligibility by a spine-specialist physician. The presence of a herniated lumbar disk was established by concordance between 2 independent readings of the patient's lumbar spine MRI by 2 spine physicians or a spine physician and a neuroradiologist.

Randomization was performed using variable block sizes and implemented by the University of California, San Francisco Compounding Pharmacy, which provided prefilled medication bottles according to a randomization list generated by nonstudy personnel. Study investigators, staff, and participants were blinded to treatment assignment.

Participants were seen in the clinic at 3 weeks and 24 weeks after randomization and were telephoned at 6, 12, and 52 weeks. By protocol, patients who did not describe themselves as at least “much better” on the patient global assessment item and whose ODI score remained higher than 30 points were offered ESIs at 3 and 6 weeks after randomization but could also be referred for an ESI by their physician at any time.

The occurrence of adverse events was ascertained at each study contact. Study progress was reviewed regularly by a data and safety monitoring board constituted by the National Institute of Arthritis and Musculoskeletal and Skin Diseases. All study procedures were approved by the institutional review board of the Kaiser Foundation Research Institute; written informed consent was obtained from all participants.

The first participant was randomized in November 2008; the last participant assessment occurred in August 2013.

Statistical Analysis

The trial had sufficient statistical power for a 90% probability of detecting a difference of 7.0 points or more on the ODI at 3 weeks, assuming a standard deviation in ODI scores of 15.1, with a randomization ratio of 2:1 and a 2-sided α=.047 (to allow for up to 2 interim analyses).[20] The intergroup difference of 7.0 points was within the range of published estimates of the minimum clinically important difference for the ODI.[21-28] These calculations required an evaluable sample of 226 participants; assuming a potential 20% withdrawal rate, the final intended sample size was 270 participants.

Unadjusted analyses were conducted using the *t* test for continuous and ordinal variables and were consistent with the corresponding Wilcoxon rank sum tests. Categorical variables (including the responder analyses) were analyzed with the Fisher exact test or its generalization for more than 2 levels.[29] Adjusted analyses for continuous and ordinal variables were conducted with multivariable linear regression models, assessed for model fit and departures from the modeling assumptions. For dichotomous outcome variables, adjusted risk ratios were obtained from multivariable Poisson regression models using robust (Huber-White) standard errors.[30] The final models included adjustments for baseline demographics, study site, presence of a positive straight-leg raise test result at baseline, and elapsed time between symptom onset and randomization. Continuous outcomes were dichotomized at several cut points for a set of exploratory, post hoc responder analyses. All analyses were conducted under the principle of intention to treat in that all participants were analyzed in the group to which they were randomized, regardless of adherence. For the 52-week data, all models were fit to 50 multiple-imputed data sets using a Markov chain Monte Carlo method.[31] All reported *P* values are 2-sided, with $P < .05$ signifying statistical significance, and no adjustments were made for multiple hypothesis testing. All analyses were conducted with Stata software, version 13.1.[31]

Seven subgroup analyses were prespecified (numbers in each group shown in brackets): median baseline severity of symptoms (ODI score ≤48 vs >48 [n=140 vs n=129]), presence of baseline ipsilateral motor weakness (muscle strength score 0-3 vs 4-5 on a 0- to 5-point scale, with higher scores indicating greater strength [n=14 vs n=255]), median time between onset of symptoms and randomization (≤25 days vs >25 days [n=137 vs n=132]), median age (≤46 vs >46 years [n=137 vs n=132]), sex (male vs female [n=149 vs n=120]), race (white vs nonwhite [n=179 vs n=90]), and ethnicity (Hispanic vs non-Hispanic [n=62 vs n=207]). Other subgroups examined were median baseline pain score (≤6 vs >6 [n=107 vs n=162]) and straight-leg raise test (positive vs negative result [n=224 vs n=45]). All subgroup analyses were performed using interaction terms in the multivariable regression models.

Results

Of the 543 individuals screened, 269met eligibility criteria and were enrolled (Figure 1). The most common reasons for ineligibility were related to age, radiographic findings, severity or duration of symptoms, or current steroid treatment.

Treatment groups were generally well matched at baseline (Table 1), although participants randomized to prednisone included a higher prevalence of white patients and a lower prevalence of reporting more than 1 race, declining to state a race, and Hispanic ethnicity.

The primary outcome visit at 3 weeks was attended by 267 participants (99.3%), and the secondary 52-week outcome assessment was completed by 234 participants (87.0%). Two hundred fifty-four (95.5%) of 266 participants for whom adherence data were available took all their study medication and 263 (98.9%) took at least 75% of their study medication.

Participants in both blinded treatment groups showed an improvement in symptoms over the initial 6 weeks, with more gradual reductions until the 24-week visit, after which changes were more variable (Figure 2). Baseline ODI scores were 51.2 and 51.1 in the prednisone and placebo groups, respectively; corresponding ODI scores at 3 weeks were 32.2 and 37.5. At 3 weeks, participants in the prednisone-treated group showed an unadjusted mean 5.6-point (95%CI, 1.1-10.1; $P = .01$) greater reduction in ODI scores compared with participants in the placebo group (Figure 2A). At 52 weeks, the mean between-group difference was 7.6 points (95%CI, 2.6-12.7; $P = .003$). After statistical adjustment, the between-group differences also favored prednisone at 3 weeks (mean difference, 6.4 points; 95% CI, 1.9-10.9; $P = .006$) and at 52 weeks (mean difference, 7.4 points; 95% CI, 2.2-12.5; $P = .005$) (Table 2).

In a responder analysis, the prednisone-treated group showed a significantly greater relative likelihood of achieving at least a 30-point or 50% improvement in the ODI at 3 weeks (relative risk [RR], 1.7; 95% CI, 1.1-2.9; number needed to treat [NNT], 10.6 and RR, 1.8; 95% CI, 1.1-2.9; NNT, 7.6, respectively) and at 52 weeks (RR, 1.3; 95% CI, 1.0-1.6; NNT, 7.1 and RR, 1.2; 95% CI, 1.1-1.5; NNT, 5.5, respectively) (Table 2).

Unlike the ODI, there was no statistically significant difference between groups in changes in the below-waist pain NRS at either the 3-week or 52-week time points (Table 2 and

Figure 2B). Similarly, there were no significant differences between groups in the proportion of participants achieving at least a 2-, 3-, or 5-point improvement in the pain NRS scores at either time point (Table 2).

Participants randomized to prednisone had a significantly greater improvement in the Physical Component Summary score of the Short Form 36 at 3 weeks (by a mean of 3.3 points; 95% CI, 1.3-5.2; $P = .001$) and the Mental Component Summary score at 1 year (by a mean of 3.6 points; 95%CI, 0.6- 6.7; $P = .02$) (Table 2).

Over the 1-year follow-up period, there was no significant between-group difference in the likelihood of undergoing spine surgery (9.9% vs 9.1%; RR, 1.2; 95%CI, 0.5-2.6; $P = .68$) (Table 2).

The global patient assessment outcome, an exploratory outcome, was measured with a dynamic perceived change in leg pain score. Between-group differences favored the prednisone group, in whom the change was significantly greater at the 3-week visit (Table 2).

Subgroup analyses revealed no statistically significant interactions at either the 3-week or 52-week time points in the between-group changes in the ODI or pain NRS with baseline age, sex, race, ethnicity, elapsed time between onset of symptoms and randomization, lower extremity motor weakness, or presence of a positive straight-leg raise test result.

By the 3-week visit, 88 participants (49.2%) in the prednisone group reported at least 1 adverse event compared with 21 (23.9%) randomized to placebo ($P < .001$). The majority (82.1%) of these were minor, expected adverse effects commonly associated with short courses of prednisone, such as insomnia, nervousness, and increased appetite (Table 3). By the 52-week visit, 208 participants (77.3%) reported a total of 723 adverse events; there were no significant differences in the mean number of adverse events per person in the active- and placebo-treated groups (2.70 vs 2.69; $P = .98$) or in the proportion of participants in each group reporting at least 1 adverse event (80.1% vs 71.6%; $P = .12$). Overall, 5 serious adverse events occurred over the 52-week follow-up period, 3 in the prednisone group (appendectomy, suicide attempt, and deep venous thrombosis) and 2 in the placebo group (upper gastrointestinal tract hemorrhage and partial nephrectomy for renal cell carcinoma); none was judged to be likely due to the study medication.

At the 3-week time point, 130 (74.7%) participants in the prednisone group believed that they had been given the active treatment compared with 48 (52.8%) of placebo-assigned participants ($P = .001$).

Discussion

Acute lumbar radiculopathy associated with a herniated nucleus pulposus commonly causes substantial pain and disability and generates significant costs.[3,4,32] Treatment options include advice, education, self care, and medications (including oral steroids), followed by various physical modalities (eg, physical therapy, ultrasound, electrical stimulation), epidural steroids, and micro diskectomy if pain persists.[3,7,8,33,34]

Over the past 35 years, 6 comparative trials have studied the use of nonepidural steroids in patients with sciatica.[35-40] These trials were generally small with low statistical power (3 enrolled fewer than 40 patients[36,37,39]). Most of these studies did not find evidence of efficacy of steroid treatment, although 1 recent trial (which enrolled the greatest number of participants) found a trend toward improvement in pain and a significant benefit in function 1 month after a single intramuscular injection of methylprednisolone.[40] To date, however, no study has examined the effectiveness of a full course of oral steroids in addition to usual care in a well-powered clinical trial.

In this trial of oral prednisone for patients with acute lumbar radiculopathy, we found a small, statistically significant improvement in function (as measured by the ODI) at both 3 weeks and 52 weeks favoring the prednisone-treated group but no difference in lower extremity pain scores at any time point. Several secondary outcomes showed small but inconsistent improvements in the active treatment group relative to the placebo group. Interaction analyses did not reveal any subgroup response that might explain these results. There was no significant difference in the likelihood of undergoing spine surgery up to 52 weeks. While there were significantly more adverse effects in the treatment group noted at 3 weeks, these were primarily transient, expected adverse effects associated with short courses of oral prednisone and there was no difference in adverse events at 1 year; no serious adverse events related to treatment were observed.

The adjusted mean improvement for the primary functional outcome, the ODI, was 6.4 points on a 100-point scale 3 weeks following randomization. This degree of benefit must be interpreted in the context of the clinical setting, as there is no clear consensus regarding the patient-relevant minimum clinically important difference for the ODI, with most published estimates in the range of 5 to 15 points.[21-28] We designed the study power calculations around a minimum clinically important difference of 7 points, which was chosen to be in the lower end of this interval, although this choice was arbitrary, given the lack of published consensus. Whether the observed improvement in function (without concomitant improvement in pain) merits use of oral steroids for patients with an acute radiculopathy is a difficult decision and, ultimately, becomes a personal one that must be weighed by individual patients and their physicians. In addition, pain may limit function, so as pain decreases, function (ODI) may increase until pain again limits functional capacity. This may explain the improved function without measurable improvement in pain.

Examination of the response curves (Figure 2) for both the ODI and pain NRS show that the small between-group differences observed 3 weeks after randomization were not observed at the 6-week time point. However, between-group differences were statistically significant again at the 52-week follow-up. The magnitude of the difference at the 52-week follow-up is greater than the magnitude of the difference at the 3-week follow-up. We know of no physiological explanation for a potential delayed effect of prednisone. The observed difference at the 52-week follow-up may be due to chance.

An important rationale for using oral steroids is the potential to decrease the need for more invasive interventions. However, in this trial, the use of prednisone did not decrease the likelihood of undergoing surgery.

Our study had several strengths, including effective randomization, high adherence to the intervention, high follow-up rates, and use of standardized patient-reported outcomes. Several potential limitations should also be noted. While it is possible that allowing upto 3 months after onset of symptoms was too long, we did not find any significant difference in response based on the time to treatment. We chose what we considered to be an adequate dosage for the prednisone treatment, but it may be argued that this dosage was insufficient. Blinding was only partially successful, probably because of the common adverse effects of oral steroids. Although we had multiple secondary outcomes, we did not adjust for multiple comparisons. In addition, generalizability of our results may be limited by the requirement for a positive MRI finding and a baseline ODI score of 30 points or higher.

Conclusions

Among patients with acute radiculopathy due to a herniated lumbar disk, a short course of oral steroids, compared with placebo, resulted in modest improvement in function and no significant improvement in pain.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Frymoyer JW. Back pain and sciatica. N Engl J Med. 1988; 318(5):291–300. [PubMed: 2961994]
2. Kreiner DS, Hwang SW, Easa JE, et al. North American Spine Society. An evidence-based clinical guideline for the diagnosis and treatment of lumbar disc herniation with radiculopathy. Spine J. 2014; 14(1):180–191. [PubMed: 24239490]
3. Koes BW, van Tulder MW, Peul WC. Diagnosis and treatment of sciatica. BMJ. 2007; 334(7607): 1313–1317. [PubMed: 17585160]
4. Valat J-P, Genevay S, Marty M, Rozenberg S, Koes B. Sciatica. Best Pract Res Clin Rheumatol. 2010; 24(2):241–252. [PubMed: 20227645]
5. Konstantinou K, Dunn KM. Sciatica: review of epidemiological studies and prevalence estimates. Spine (Phila Pa 1976). 2008; 33(22):2464–2472. [PubMed: 18923325]
6. Weber H, Holme I, Amlie E. The natural course of acute sciatica with nerve root symptoms in a double-blind placebo-controlled trial evaluating the effect of piroxicam. Spine (Phila Pa 1976). 1993; 18(11):1433–1438. [PubMed: 8235813]
7. Weinstein JN, Tosteson TD, Lurie JD, et al. Surgical vs nonoperative treatment for lumbar disk herniation: the Spine Patient Outcomes Research Trial (SPORT): a randomized trial. JAMA. 2006; 296(20):2441–2450. [PubMed: 17119140]
8. Pinto RZ, Maher CG, Ferreira ML, et al. Epidural corticosteroid injections in the management of sciatica: a systematic review and meta-analysis. Ann Intern Med. 2012; 157(12):865–877. [PubMed: 23362516]

9. Olmarker K, Byröd G, Cornefjord M, Nordborg C, Rydevik B. Effects of methylprednisolone on nucleus pulposus-induced nerve root injury. Spine (Phila Pa 1976). 1994; 19(16):1803–1808. [PubMed: 7973978]
10. Cohen SP, White RL, Kurihara C, et al. Epidural steroids, etanercept, or saline in subacute sciatica: a multicenter, randomized trial. Ann Intern Med. 2012; 156(8):551–559. [PubMed: 22508732]
11. Kobayashi S, Baba H, Uchida K, et al. Effect of mechanical compression on the lumbar nerve root: localization and changes of intraradicular inflammatory cytokines, nitric oxide, and cyclooxygenase. Spine (Phila Pa 1976). 2005; 30(15):1699–1705. [PubMed: 16094269]
12. Center for Drug Evaluation and Research. [September 15, 2014] FDA Drug Safety Communication: FDA requires label changes to warn of rare but serious neurologic problems after epidural corticosteroid injections for pain. Apr 23. 2014 http://www.fda.gov/Drugs/DrugSafety/ucm394280.htm
13. Manchikanti L, Candido KD, Singh V, et al. Epidural steroid warning controversy still dogging FDA. Pain Physician. 2014; 17(4):E451–E474. [PubMed: 25054397]
14. Wong, DA., Mayer, TG., Watters, WC., Sims, WA., Spivak, JM., Brant-Zawadzki, M. Oral Steroids: North American Spine Society Phase III Clinical Guidelines for Multidisciplinary Spine Care Specialists. Vol. 41. LaGrange, IL: North American Spine Society; 2002.
15. Luke, A., Ma, B. Lumbar disk herniation in sports medicine and outpatient orthopedics. In: Papadakis, M., McPhee, S., editors. Current Medical Diagnosis and Treatment. New York, NY: McGraw-Hill Medical Books; 2015.
16. Levin, K., Hsu, P., Armon, C. Acute Lumbosacral Radiculopathy: Prognosis and Treatment. Waltham, MA: UpToDate; 2014.
17. Roncoroni C, Baillet A, Durand M, Gaudin P, Juvin R. Efficacy and tolerance of systemic steroids in sciatica: a systematic review and meta-analysis. Rheumatology (Oxford). 2011; 50(9):1603–1611. [PubMed: 21525139]
18. Fairbank JCT. Why are there different versions of the Oswestry Disability Index? J Neurosurg Spine. 2014; 20(1):83–86. [PubMed: 24206036]
19. Ware, JE., Kosinski, M., Dewey, JE. How to Score Version Two of the SF-36 Health Survey. Lincoln, RI: QualityMetric Inc; 2000.
20. O'Brien PC, Fleming TR. A multiple testing procedure for clinical trials. Biometrics. 1979; 35(3): 549–556. [PubMed: 497341]
21. Fritz JM, Irrgang JJ. A comparison of a modified Oswestry Low Back Pain Disability Questionnaire and the Quebec Back Pain Disability Scale. Phys Ther. 2001; 81(2):776–788. [PubMed: 11175676]
22. Hägg O, Fritzell P, Nordwall A. Swedish Lumbar Spine Study Group. The clinical importance of changes in outcome scores after treatment for chronic low back pain. Eur Spine J. 2003; 12(1):12–20. [PubMed: 12592542]
23. Childs JD, Piva SR. Psychometric properties of the functional rating index in patients with low back pain. Eur Spine J. 2005; 14(10):1008–1012. [PubMed: 15834591]
24. Lauridsen HH, Hartvigsen J, Manniche C, Korsholm L, Grunnet-Nilsson N. Responsiveness and minimal clinically important difference for pain and disability instruments in low back pain patients. BMC Musculoskelet Disord. 2006; 7:82. [PubMed: 17064410]
25. Mannion AF, Junge A, Fairbank JC, Dvorak J, Grob D. Development of a German version of the Oswestry Disability Index, I: cross-cultural adaptation, reliability, and validity. Eur Spine J. 2006; 15(1):55–65. [PubMed: 15856341]
26. Ostelo RW, Deyo RA, Stratford P, et al. Interpreting change scores for pain and functional status in low back pain: towards international consensus regarding minimal important change. Spine (Phila Pa 1976). 2008; 33(1):90–94. [PubMed: 18165753]
27. Copay AG, Glassman SD, Subach BR, Berven S, Schuler TC, Carreon LY. Minimum clinically important difference in lumbar spine surgery patients: a choice of methods using the Oswestry Disability Index, Medical Outcomes Study questionnaire Short Form 36, and pain scales. Spine J. 2008; 8(6):968–974. [PubMed: 18201937]
28. Cleland JA, Whitman JM, Houser JL, Wainner RS, Childs JD. Psychometric properties of selected tests in patients with lumbar spinal stenosis. Spine J. 2012; 12(10):921–931. [PubMed: 22749295]

29. Mehta CR, Patel NR. A network algorithm for performing Fisher's exact test in r_c contingency tables. J Am Stat Assoc. 1983; 78:427–434.
30. Zou G. A modified Poisson regression approach to prospective studies with binary data. Am J Epidemiol. 2004; 159(7):702–706. [PubMed: 15033648]
31. Stata Corp. Stata Release 13 [statistical software]. College Station, TX: Stata Corp; 2013.
32. van Tulder MW, Koes BW, Bouter LM. A cost-of-illness study of back pain in the Netherlands. Pain. 1995; 62(2):233–240. [PubMed: 8545149]
33. Chou R, Huffman LH. American Pain Society; American College of Physicians. Medications for acute and chronic low back pain: a review of the evidence for an American Pain Society/American College of Physicians clinical practice guideline. Ann Intern Med. 2007; 147(7):505–514. [PubMed: 17909211]
34. Jacobs WCH, van Tulder M, Arts M, et al. Surgery vs conservative management of sciatica due to a lumbar herniated disc: a systematic review. Eur Spine J. 2011; 20(4):513–522. [PubMed: 20949289]
35. Porsman O, Friis H. Prolapsed lumbar disc treated with intramuscularly administered dexamethasone phosphate: a prospectively planned, double-blind, controlled clinical trial in 52 patients. Scand J Rheumatol. 1979; 8(3):142–144. [PubMed: 386492]
36. Hedeboe J, Buhl M, Ramsing P. Effects of using dexamethasone and placebo in the treatment of prolapsed lumbar disc. Acta Neurol Scand. 1982; 65(1):6–10. [PubMed: 7039210]
37. Haimovic IC, Beresford HR. Dexamethasone is not superior to placebo for treating lumbosacral radicular pain. Neurology. 1986; 36(12):1593–1594. [PubMed: 2946981]
38. Finckh A, Zufferey P, Schurch M-A, Balagué F, Waldburger M, So AKL. Short-term efficacy of intravenous pulse glucocorticoids in acute discogenic sciatica: a randomized controlled trial. Spine (Phila Pa 1976). 2006; 31(4):377–381. [PubMed: 16481946]
39. Holve RL, Barkan H. Oral steroids in initial treatment of acute sciatica. J Am Board Fam Med. 2008; 21(5):469–474. [PubMed: 18772303]
40. Friedman BW, Esses D, Solorzano C, et al. A randomized placebo-controlled trial of single-dose IM corticosteroid for radicular low back pain. Spine (Phila Pa 1976). 2008; 33(18):E624–E629. [PubMed: 18665021]

Glossary

ESI	epidural steroid injection
MRI	magnetic resonance imaging
NRS	numerical rating scale
ODI	Oswestry Disability Index

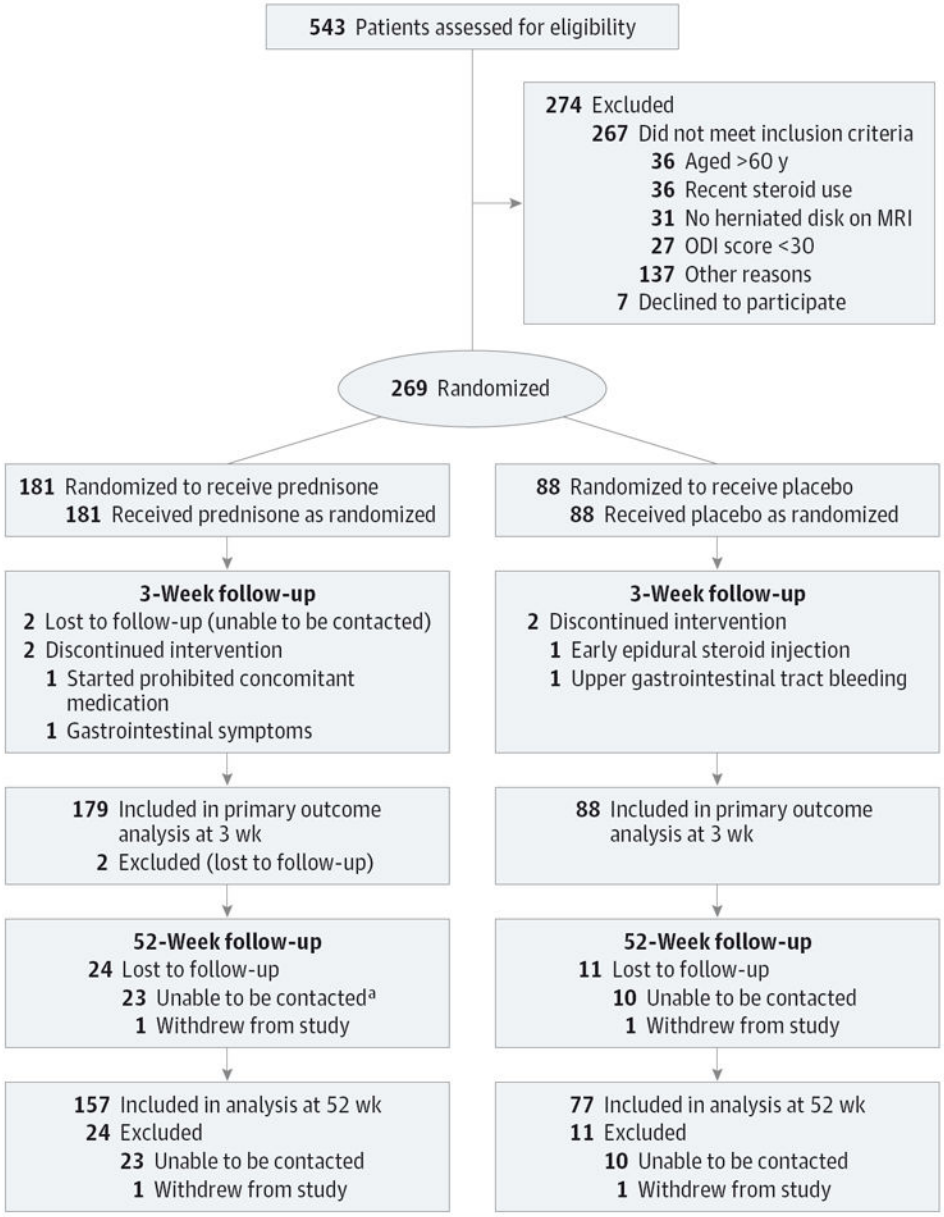

Figure 1. Flow of Participants in Randomized, Double-Blind Trial of Oral Prednisone vs Placebo Through 3-Week (Primary) and 52-Week (Secondary) Follow-up

MRI indicates magnetic resonance imaging; ODI, Oswestry Disability Index.

[a] One of the 2 participants lost to 3-week follow-up visits was lost to follow-up for the entire study after the baseline visit. The other participant was contacted and included in the final 52-week follow-up.

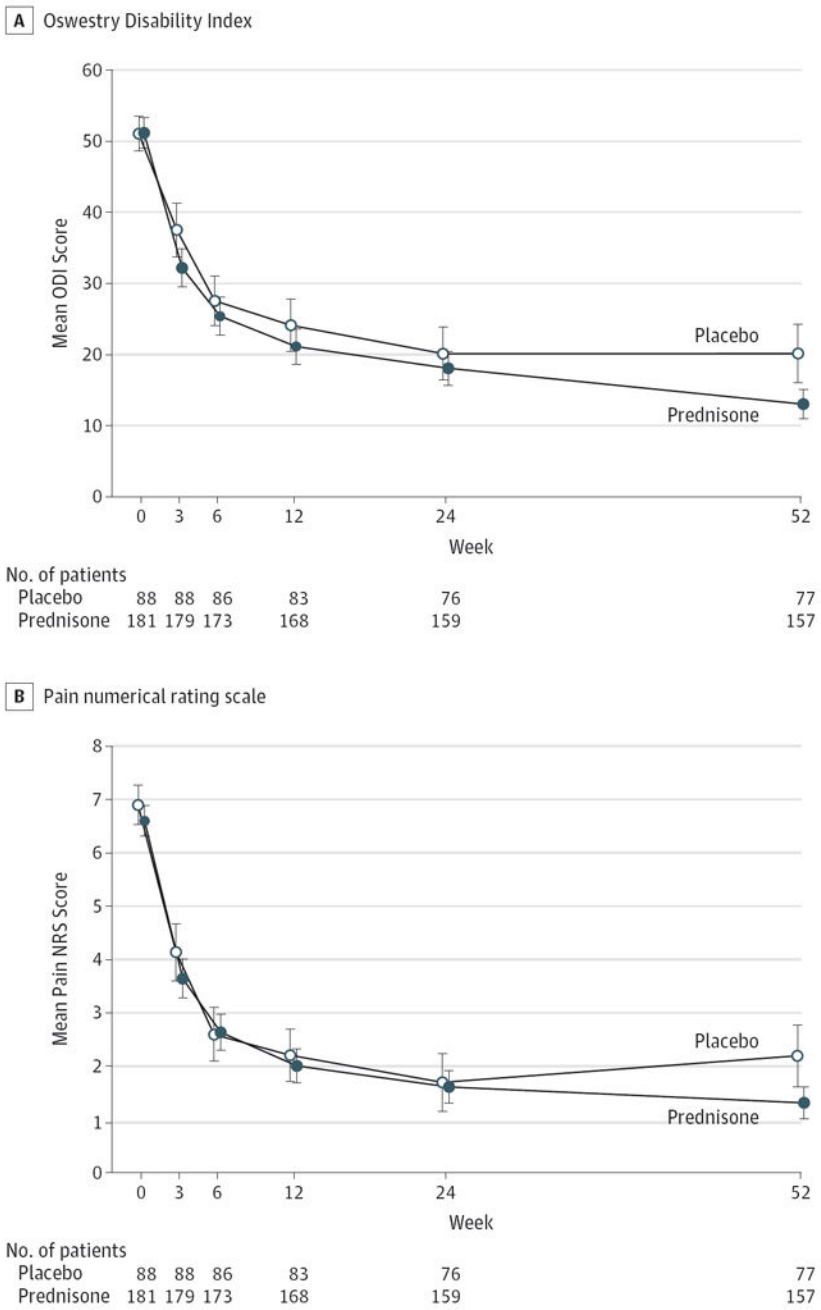

Figure 2. Scores on the Oswestry Disability Index and Pain Numerical Rating Scale

Observed mean values for the (A) Oswestry Disability Index (ODI) and (B) pain numerical rating scale (NRS) for average pain below the waist in the prior 3 days in the prednisone-treated and placebo-treated groups. The ODI is measured on a 0- to 100-point scale, with higher numbers indicating more functional disability. The pain NRS is measured on a 0- to 10-point scale, with higher numbers indicating more pain. Treatment occurred during the first 15 days after randomization. Errors bars indicate 95% CIs.

Table 1

Baseline Demographic and Clinical Characteristics Overall and by Study Group

Characteristics	All Participants (N = 269)	Prednisone Group (n = 181)	Placebo Group (n = 88)
Age, mean (SD), y	46.0 (12.1)	45.6 (11.8)	46.7 (12.6)
Male, No. (%)	149 (55.4)	98 (54.1)	51 (58.0)
Race, No. (%)[a]			
Native American	5 (1.9)	1 (0.6)	4 (4.6)
Asian	32 (11.9)	24 (13.3)	8 (9.1)
African American	6 (2.2)	3 (1.7)	3 (3.4)
Pacific Islander	2 (0.7)	2 (1.1)	0
White	179 (66.5)	129 (71.3)	50 (56.8)
>1 Race	19 (7.1)	10 (5.5)	9 (10.2)
Declined to state race	26 (9.7)	12 (6.6)	14 (15.9)
Ethnicity, No. (%)[b]			
Hispanic	62 (23.1)	34 (18.8)	28 (31.8)
Education, No. (%)			
High school graduate or lower	68 (25.3)	46 (25.4)	22 (25.0)
Some college	95 (35.3)	65 (35.9)	30 (34.1)
College graduate or higher	106 (39.4)	70 (38.7)	36 (40.9)
Oswestry Disability Index score, mean (SD)[c]	51.1 (13.5)	51.2 (14.5)	51.1 (11.5)
Below-waist pain numerical rating scale score, mean (SD)[d]	6.7 (1.9)	6.6 (2.0)	6.9 (1.8)
Time from pain onset to randomization, d			
Mean (SD)	30.4 (21.4)	29.7 (20.8)	31.7 (22.7)
Median (interquartile range)	25 (14-42)	25 (14-38)	27 (12-48)
Positive straight-leg raise test result, No. (%)	224 (88.4)	154 (85.1)	70 (79.6)
Muscle weakness at baseline, No. (%)[e]	14 (5.2)	8 (4.4)	6 (6.8)
Short Form 36 Health Survey score, mean (SD)			
Physical Component Summary[f]	30.6 (6.6)	30.4 (6.8)	30.9 (6.2)
Mental Component Summary[g]	48.7 (11.8)	48.5 (11.6)	49.3 (12.3)

[a] P=.009 for prednisone group vs placebo group.

[b] P=.02 for prednisone group vs placebo group.

[c] Score range, 0-100; higher scores indicate greater dysfunction.

[d] Score range, 0-10; higher scores indicate more pain.

[e] Defined as score ≤3 on 0- to 5-point scale for lower extremity motor strength scoring.

[f] Score range, 0-100; higher scores indicate better physical health status.

[g] Score range, 0-100; higher scores indicate better mental health status.

Table 2

Changes in Outcome Measures From Baseline to 3-Week and 52-Week Follow-up

Outcomes	3-Week Follow-up				52-Week Follow-up			
	Prednisone Group (n = 179)	Placebo Group (n = 88)	Adjusted Difference Between Groups (95% CI)[a]	*P* Value	Prednisone Group (n = 157)	Placebo Group (n = 77)	Adjusted Difference Between Groups (95% CI)[a]	*P* Value
Primary outcome, mean (95% CI)								
Oswestry Disability Index Score[b]	−19.0 (−21.6 to −16.3)	−13.3 (−16.7 to −10.0)	−6.4 (−10.9 to −1.9)	.006	.006 −37.8 (−40.7 to −35.0)	−30.4 (−34.8 to −25.9)	−7.4 (−12.5 to −2.2)	.005
Other continuous outcomes, mean (95% CI)								
Pain numerical rating scale Score[c]								
Below waist, average	−3.0 (−3.3 to −2.6)	−2.8 (−3.3 to −2.2)	−0.3 (−1.0 to 0.4)	.34	−5.2 (−5.6 to −4.7)	−4.6 (−5.2 to −4.0)	−0.6 (−1.3 to 0.2)	15
Below waist, worst	−3.6 (−4.0 to −3.1)	−3.2 (−3.8 to −2.6)	−0.5 (−1.3 to 0.3)	.20	−6.5 (−7.0 to −6.1)	−5.7 (−6.4 to −5.0)	−0.7 (−1.6 to 0.1)	.09
Below waist, least	−2.0 (−2.4 to −1.6)	−1.5 (−2.1 to −1.0)	−0.5 (−1.2 to 0.2)	.13	−3.4 (−3.8 to −2.9)	−3.0 (−3.6 to −2.3)	−0.4 (−1.1 to 0.4)	33
Above waist, average	−1.0 (−1.3 to −0.6)	−0.8 (−1.3 to −0.3)	−0.2 (−0.8 to 0.5)	.65	−1.5 (−2.0 to −1.0)	−1.4 (−2.0 to −0.7)	−0.2 (−1.0 to 0.6)	.61
Short Form 36 Health Survey score[d]								
Physical Component Summary	5.8 (4.7 to 7.0)	2.8 (1.3 to 4.2)	3.3 (1.3 to 5.2)	.001	18.0 (16.5 to 19.5)	15.7 (13.2 to 18.2)	2.5 (−0.3 to 5.4)	.08
Mental Component Summary	1.2 (−0.2 to 2.6)	−0.7 (−3.0 to 1.6)	2.2 (−0.4 to 4.8)	.10	6.9 (5.1 to 8.7)	3.1 (0.7 to 5.4)	3.6 (0.6 to 6.7)	.02
Categorical outcomes, No. (%) [95% CI]								

Outcomes	3-Week Follow-up				52-Week Follow-up			
	Prednisone Group (n = 179)	Placebo Group (n = 88)	Adjusted Difference Between Groups (95% CI)[a]	*P* Value	Prednisone Group (n = 157)	Placebo Group (n = 77)	Adjusted Difference Between Groups (95% CI)[a]	*P* Value
Improvement in Oswestry Disability Index score								
≥10 points	119 (66.5) [59.5-73.4]	47 (54.7) [43.9-65.4]	1.3 (1.0-1.6)[e]	.04	148 (94.3) [90.6-97.9]	67 (88.2) [80.7-95.6]	1.1 (1.0-1.1)[e]	.24
≥15 points	97 (54.2) [46.8-61.6]	39 (45.3) [34.6-56.1]	1.2 (0.9-1.6)[e]	.14	145 (92.4) [88.1-96.6]	62 (81.6) [72.7-90.5]	1.1 (1.0-1.3)[e]	.05
≥30 points	48 (26.8) [20.2-33.4]	15 (17.4) [9.3-25.6]	1.7 (1.1-2.9)[e]	.03	111 (70.7) [63.5-77.9]	43 (56.6) [45.2-68.0]	1.3 (1.0-1.6)[e]	.04
≥50%	59 (33.0) [26.0-39.9]	17 (19.8) [11.2-28.4]	1.8 (1.1-2.9)[e]	.01	136 (86.6) [81.2-92.0]	52 (68.4) [57.7-79.1]	1.2 (1.1-1.5)[e]	.01
Improvement in pain numerical rating scale score								
≥2 points	120 (67.0) [60.1-74.0]	57 (64.8) [54.6-75.0]	1.1 (0.9-1.3)[e]	.60	141 (89.8) [85.0-94.6]	66 (85.7) [77.7-93.7]	1.0 (0.9-1.2)[e]	.45
≥3 points	92 (51.4) [44.0-58.8]	45 (51.1) [40.5-61.8]	1.0 (0.8-1.3)[e]	.85	131 (83.4) [77.6-89.3]	60 (77.9) [68.4-87.4]	1.1 (0.9-1.2)[e]	.39
≥5 points	51 (28.4) [21.8-35.2]	23 (26.1) [16.8-35.5]	1.1 (0.8-1.7)[e]	.52	106 (67.5) [60.1-74.9]	44 (57.1) [45.8-68.4]	1.2 (0.9-1.4)[e]	.19
Back surgery, any					18 (9.9) [5.5-14.3]	8 (9.1) [3.0-15.2]	1.2 (0.5-2.6)[e]	.68
Global patient assessment at least “somewhat better”	147 (82.1) [76-88]	61 (69.3) [60-79]	1.2 (1.0-1.4)[e]	.02	143 (91.1) [86.6-95.6]	66 (85.7) [77.7-93.7]	1.1 (1.0-1.2)[e]	.30

[a]Between-group differences are adjusted for baseline age, sex, race, ethnicity, study site, presence of a positive straight-leg raise test result at baseline, and elapsed time between symptom onset and randomization.

[b]Score range, 0-100; higher scores indicate greater dysfunction.

[c]Score range, 0-10; higher scores indicate more pain. Average = pain on average over past 3 days; worst = pain at its worst over past 3 days; least = pain at its least (best) over past 3 days.

[d]Score range, 0-100; higher scores indicate better physical/mental health status.

[e]Data are relative risk (95%CI).

[f] Global patient assessment was queried as "How has your leg pain changed since you started taking your study medication?" using the following ordered response categories: very much better, much better, somewhat better, about the same, somewhat worse, much worse, or very much worse.

Table 3

Adverse Events Reported by Participants Up to the 3-Week Follow-up Visit

Adverse Events[a]	All Participants, No. (%) (n = 267)[b]	Prednisone Group, No. (%) (n = 179)[c]	Placebo Group, No. (%) (n = 88)[c]
Insomnia	55 (15.9)	46 (25.7)	9 (10.2)[d]
Nervousness	40 (11.5)	33 (18.4)	7 (8.0)[e]
Increased appetite	49 (14.1)	40 (22.3)	9 (10.2)[f]
Indigestion	26 (7.5)	20 (11.2)	6 (6.8)
Headache	45 (13.0)	32 (17.9)	13 (14.8)
Joint pain	20 (5.8)	10 (5.6)	10 (11.4)
Sweating	50 (14.4)	35 (19.6)	15 (17.0)
Other	62 (17.9)	46 (25.7)	16 (18.2)
Total reporting ≥1 adverse event	106 (39.7)	88 (49.2)	21 (23.9)[g]

[a] Participants could report more than 1 event at a time. All events except “other” were assessed with a questionnaire; events noted as “other” were volunteered by participants.

[b] Percentage of all reported adverse events.

[c] Percentages of individual adverse events reported in each treatment group.

[d] $P=.003$ for prednisone group vs placebo group.

[e] $P=.03$ for prednisone group vs placebo group.

[f] $P=.02$ for prednisone group vs placebo group.

[g] $P < .001$ for prednisone group vs placebo group.