

Epidural Steroid or Etanercept Injections Have Limited to No Benefit for Subacute Sciatica

Cohen S, White R, Kurlhara C, et al. Epidural steroids, etanercept, or saline in subacute sciatica: a multicenter, randomized trial. *Ann Intern Med* 2012;156:551–9.

Study Overview

Objective. To determine whether epidural steroid or etanercept injections compared with saline improve symptoms from subacute sciatica.

Design. Randomized, double-blind, placebo-controlled trial. Subjects received 2 epidural injections, separated by 2 weeks, of either etanercept, an inhibitor of tumor necrosis factor, steroids, or saline, all mixed with bupivacaine, and were followed for up to 6 months.

Setting and participants. 84 adults from 6 clinical sites (4 military and 2 civilian) with lumbosacral radiculopathy (“sciatica”). The study included subjects aged 18 to 70 years with sciatica for 4 weeks to 6 months who had more leg than back pain, failed conservative therapy, and had MRI evidence of either a herniated disc or annular tear that anatomically correlated with their reported symptoms. Exclusions included a coagulopathy, systemic infection, any unstable medical or psychiatric diagnosis, a history of spinal surgery or an epidural steroid injection, or a contrast allergy. At the time of the injections, subjects were instructed to use opiates, NSAIDs, or tramadol for additional pain control.

Main outcome measures. Leg pain, rated on a 0–10 scale, at 1 month post-injection. Secondary outcomes included back pain 1 month post-injection (rated on a 0–10 scale), disability (rated using the Oswestry Disability Index), reduction in analgesics, and a global perceived effect (GPE) of the treatment (“my pain has improved/worsened/stayed the same” and “I am satisfied/not satisfied with the treatment”), all measured at 1 month.

Main results. The average age of subjects was 42.3 years; average duration of pain was nearly 3 months. Over 60% were male in each group. Leg pain was moderate to high at the time of enrollment, with a mean of 6.2 (SD 1.9) on the 10-point scale. All subjects improved by 1 month

after treatment, with reductions of leg pain of -3.57 (95% confidence interval [CI] -4.43 to -2.71) among those receiving steroids, -2.98 (95% CI -4.41 to -1.55) among those receiving etanercept, and -2.48 (95% CI -3.59 to -1.37) among those receiving saline. Decreases in back pain were less substantial but statistically significant. For functional capacity, subjects receiving steroids or saline noted significant improvements whereas subjects receiving etanercept did not. Subjects receiving steroid injections had a small but nonsignificant decrease in leg pain (mean difference on pain scale of -1.26 , 95% CI -2.79 to 0.27 , $P = 0.11$), back pain (-0.52 , 95% CI -1.85 to 0.81 , $P = 0.44$) and functional capacity (-5.87 , 95% CI -15.59 to 3.85 , $P = 0.23$) versus saline. Subjects receiving etanercept had similar responses for leg pain (-1.01 , 95% CI -2.60 to 0.58 , $P = 0.21$) and back pain (-0.92 , 95% CI -2.28 to 0.44 , $P = 0.18$) compared with saline and actually had worse functional capacity (10.29 , 95% CI 0.55 to 20.04 , $P = 0.04$) versus saline. Etanercept also was associated with worse functional capacity compared with steroids. One-half of all subjects decreased their analgesic use by 1 month, ranging from 63% in the steroid group to 36% in the etanercept group; however, these changes were not significant. Satisfaction on the GPE scale at 1 month was achieved by 82% in the steroid group compared with 58% and 57% in the etanercept and saline groups, again not significant. 29%, 38%, and 40% reported successful outcomes at 6 months for the steroid, etanercept, and saline recipients, respectively. Complications were minimal, and all were deemed minor.

Conclusion. Epidural steroid injections demonstrated limited improvement compared with saline for sciatica, and etanercept actually led to worse outcomes.

Commentary

The overwhelming majority of people with sciatica improve on their own, regardless of the type of treatment they receive. In a randomized controlled trial of

283 patients with severe symptoms assigned to either early surgical diskectomy vs. conservative treatment (pain management and physical therapy followed by surgery if needed; 39% eventually had surgery), 95% of all patients reported that they recovered from their symptoms by 1 year [1]. However, the high cost and burden of sciatica in the United States have led to continued efforts to find adequate successful treatments in the short and long term. Few treatments for sciatica have been found to help. Gabapentin and opiates have the best data to support an effect for sciatica, albeit relatively weak, with minimal evidence to support other treatments such as NSAIDs [2]. Surgical outcomes for herniated discs have been disappointing, especially over the long term [1,3]. Nonspecific acute back pain may benefit from NSAIDs, acetaminophen, muscle relaxers (with perhaps more benefit from nonbenzodiazepines such as cyclobenzaprine) and alternative therapies, including spinal manipulation and heat [2].

Epidural injections of steroids have become a mainstay of therapy for back pain despite limited data showing a benefit [2,4] and some concern for potential significant harm [5–7]. These injections are administered primarily for sciatica, to decrease the inflammation that results with direct disc compression on nerve roots in the lumbosacral spine. Recently, tumor necrosis factor inhibitors, used commonly for rheumatologic and other inflammatory conditions, have emerged as possible safer alternatives to steroids, when administered locally, similar to epidural steroid injections [8]. This study examined the effect of epidural steroid or etanercept versus saline for the treatment of subacute sciatica.

Evidence for benefit from either treatment (steroids or etanercept) was weak. On average, subjects receiving any of the treatments had significant improvements in leg and back pain at 1 month, and more than 50% were satisfied with the outcome at a month, declining to 29% to 40% by 6 months. The improvements in leg and back pain were not significantly different among any of the groups. Functional capacity did not improve in the etanercept group compared with the other groups; a decline in sleep and sexual function were the main reported causes of the lack of functional improvement in the etanercept group.

There were several limitations in this study, with the foremost being the small sample size. The study was powered to uncover a difference of 2 points on the 0 to 10 pain scale between the treatment groups and

placebo/saline, which is a fairly sizable difference (33% of the baseline pain level). There were some signals of more improvement in the steroid group compared with saline, which were ultimately not significant; with a larger sample, a statistically significant difference may have been seen. Further, the patient population enrolled in this intervention was rather young and healthy by design. Similar results may not be evident among a more complicated (and typical) primary care population. Authors also note that the dose of etanercept might have been too low to achieve therapeutic effect, and they call for more study of the dosing level of etanercept that might be needed to achieve success.

The authors of this study conclude that “the results of our study suggest short-term superiority but limited long-term benefit for epidural steroids compared with epidural saline” and that “epidural etanercept seemed to provide no advantages over epidural saline.” These conclusions are overly optimistic and not matched by the actual results of nonsignificant benefits of steroids versus saline. Prior reviews of efficacy and effectiveness of these injections have found similar, unconvincing results [2,4]. In fact, the burden for epidural steroid injections should be quite high, considering the significant expense of these injections. In 2007, the total cost to Medicare for transforaminal epidural steroid injections was \$141 million, compared with \$57 million in 2003 [9]. The Department of Health and Human Services also concluded in 2010 that 34% of services associated with these injections did not meet Medicare requirements, typically because of inappropriate facility payments or documentation errors [9]. If we cannot even document clear short-term superiority of this treatment versus placebo, then the use of this treatment should be viewed skeptically. Obviously, large, well-conducted trials must be completed to determine this for certain. But in the meantime, conservative therapy may remain the mainstay of treatment for sciatica, with a good expectation that improvements will be substantial regardless of whether any escalation in therapy is made.

Applications for Clinical Practice

Epidural steroid injections are not superior to saline injections in this study even over the short term. Epidural etanercept injections also were not superior and in fact led to worse functional status compared with both steroid and saline injections at 1 month. These treatments should be viewed skeptically and perhaps

reserved for cases with no improvement after conservative therapy over a several-month period.

—Review by Jason P. Block, MD, MPH

References

1. Peul WC, van Houwelingen HC, van den Hout WB, et al. Surgery versus prolonged conservative treatment for sciatica. *N Engl J Med* 2007;356:2245–56.
2. Cohen SP, Argoff CE, Carragee EJ. Management of low back pain. *BMJ* 2008;337:a2718.
3. Weinstein J, Tosteson T, Lurie J, et al. Surgical vs non-operative treatment for lumbar disk herniation: the Spine Patient Outcomes Research Trial (SPORT): a randomized trial. *JAMA* 2006; 296:2441–50.
4. Staal JB, de Bie RA, de Vet HC, et al. Injection therapy for subacute and chronic low back pain: an updated Cochrane review. *Spine (Phila Pa 1976)*.2009;34:49–59.
5. Rathmell JP, Aprill C, Bogduk N. Cervical transforaminal injection of steroids. *Anesthesiology* 2004;100:1595–600.
6. Houten JK, Errico TJ. Paraplegia after lumbosacral nerve root block: report of three cases. *Spine J* 2002;2:70–5.
7. Kennedy DJ, Dreyfuss P, Aprill CN, et al. Paraplegia following image-guided transforaminal lumbar spine epidural steroid injection: two case reports. *Pain Med* 2009;10:1389–94.
8. Cohen SP, Bogduk N, Dragovich A, et al. Randomized, double-blind, placebo-controlled, dose-response, and preclinical safety study of transforaminal epidural etanercept for the treatment of sciatica. *Anesthesiology* 2009;110:1116–26.
9. Department of Health and Human Services, Office of Inspector General. Inappropriate Medicare payments for transforaminal epidural injections services. August 2010. Accessed 3 May 2012 at <http://oig.hhs.gov/oei/reports/oei-05-09-00030.pdf>.

Copyright 2012 by Turner White Communications Inc., Wayne, PA. All rights reserved.