

Epidural Steroids, Etanercept, or Saline in Subacute Sciatica

BACKGROUND:

- It's estimated that between 37% to 55% of all cases of spinal pain are estimated to be neuropathic in origin and there is a lack of reliable treatment. Some studies have shown efficacy of epidural steroid injections, but their long-term effects are uncertain. There have also been reports of consequences related to the nature of depot steroids (i.e. spinal cord infarction, specifically with the transforaminal approach) and safer alternatives are needed. Preclinical and clinical studies have shown favorable outcomes with TNF alpha antagonists in prevention of neuropathologic activity that follows dorsal root ganglia-TNF receptor activation, such as edema formation, demyelination, and decreased conduction.

OBJECTIVE:

- To evaluate whether epidural steroids, etanercept, or saline better improves pain and function in adults with lumbosacral radiculopathy.

METHODS

- **Design:** Randomized, placebo-controlled, parallel-group trial; duration June 2008 through March 2011
- **Inclusion Criteria:** Age 18+ and <70, lumbosacral radiculopathy >4 weeks but less than or equal to 6 months in duration, leg pain that is more than or as severe as back pain, failure of conservative therapy, and evidence on MRI of pathologic disc condition correlating with symptoms (e.g. herniated disc or annular tear)
- **Exclusion criteria:** Coagulopathy, systemic infection, unstable medical or psychiatric conditions, previous spinal surgery, previous epidural steroid injection, or allergy to contrast dye
- 84 participants were separated into 1 of 3 groups and received epidural etanercept, epidural steroids, or epidural saline. Twenty-six patients that received etanercept 4mg, 28 patients received methylprednisolone 60mg, and 30 patients that received normal saline. All groups received contrast dye and 0.5mL of 0.5% bupivacaine prior to injection with study drugs
- **Primary Outcome:** A numeric rating scale (NRS) score of 0 – 10 for leg pain at 1 month that reflected the average pain the patient experienced for 1 week before follow up
- **Secondary Outcomes:** Oswestry Disability Index (ODI), which is a 10 question survey used to assess function in people with low back pain. Numeric rating scale (NRS) score of 0 – 10 for back pain during the preceding week. Reduction in analgesic medication use defined \geq 20% reduction in opioid use or cessation of nonopioid analgesics. Global perceived effect (GPE) as a positive response to the question "My pain has improved/worsened/stayed the same since my last visit" and "I am satisfied/not satisfied with the treatment I received and would recommend it to others."
- **Positive categorical outcome measure** (predefined) Reduction of 50% or more leg pain with a positive GPE, obviating the need for further intervention.
- Power 80% with 26 patients/group to detect a 2 point difference in leg pain scores between the control group and 1 or both of the treatment groups; adjusted alpha of 0.0167 to

account for comparison of 3 groups, mean baseline scale score of leg pain of 6.5, SD of 2, and a 10% dropout rate.

- Data handling method was intent-to-treat

RESULTS

- Of the 84 patients who began the study, only 10 patients declined 2nd injection b/c of lack of improvement in symptoms (n = 5) or because the patient was satisfied with pain relief (n = 5)
- **Primary Outcome Measure:** Within group changes: The largest decrease NRS for leg pain was the steroid group with a mean -3.57 (95% - 4.43 to -2.71); Etanercept -2.98 (CI -4.41 to -1.55); Saline -2.48 (CI -3.59 to -1.37. Difference between groups: NRS adjusted pain scores for leg pain were not statistically significant with steroid 2.54 (CI 1.36 to 3.69), etanercept 3.56 (CI 2.35 to 4.72), and saline 3.78 (2.72 to 4.85) P = 0.24.
- **Secondary Outcome Measure:** Within group changes: Decreased NRS for back pain was largest in the steroid group with mean decrease of -2.14 (CI -3.23 to -1.06); Etanercept -1.56 (CI -2.83 to -0.28); Saline -1.07 (CI -1.96 to -0.17). The ODI score showed sizeable improvements in the steroid group -20.50 (CI -27.70 to -13.30) and Saline -12.07 (CI -18.11 to -6.01), but not Etanercept -2.85 (CI -11.78 to 6.09). Difference between groups: the only statistically significant finding was a positive outcome on ODI scores for both the steroid and saline group. The steroid group mean score was 22.43 (SD 16.72), etanercept 38.27 (SD 24.69), and saline 28.80 (SD 21.22) with a P = 0.006.
- **The Positive Categorical Outcome Measure:** Findings were not statistically significant. There was a 50% positive categorical outcome for the etanercept group, 80% for the steroid group, and 50% for saline group; P = 0.47
- **Authors' conclusions** Principle finding is that steroids resulted in a larger reduction in leg pain than etanercept and saline for the primary outcome of leg pain at 1 month, but was not statistically significant. The ODI scores at 1 month differed statistically by group with improvements noted in the saline and steroid groups, but not etanercept. However, because of the confidence intervals for pairwise differences, these results can neither exclude nor prove a modest benefit for steroids. Concerning etanercept results were no better than saline. Dosing was based on a small pilot study calculated on the basis of formulas used for the neuraxial admin of baclofen and opioids. The low dose may have been subtherapeutic.

STRENGTHS

- Randomized, placebo-control, parallel group trial

LIMITATIONS

- They used intermediate selection criteria in a patient population largely composed of person in excellent physical condition with relatively little secondary gain (military personnel). Short term pain as the inclusion criteria versus longer term pain, which may be refractory and more difficult to treat. Other limitations include: lack of nonepidural control group, small sample sizes, relying on patient recall to record pain scores at follow-up visits, performing injections on a schedule rather than prn, the decision to allow participant with unsuccessful outcomes to discontinue the study per protocol to pursue alternative treatments

CONCLUSIONS

- Administration of epidural steroids does seem to provide a benefit in patients who have failed conservative treatments.
- There is no role for epidural etanercept at the 4 mg dose at this time
- Further research is needed in larger study samples to determine long term efficacy of epidural steroids in lumbosacral radiculopathy. In addition, safety and efficacy of etanercept at higher doses need to be done to determine optimal dosing

Reference: Cohen SP, White RL, Kurihara C, Larkin TM, *et. al.* Epidural Steroids, Etanercept, or Saline in Subacute Sciatica: A Multicenter, Randomized Trial. *Ann Intern Med.* 2012;156(8):551-9.

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