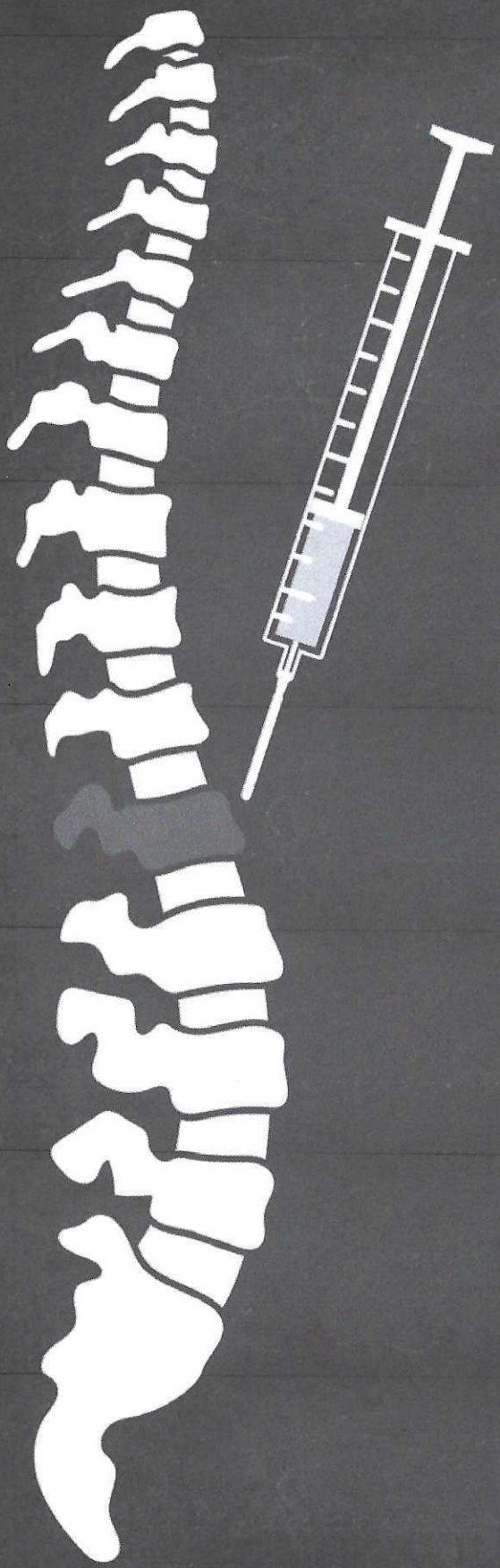


EPIDURALS (SHOTS):

Temporary Relief From Cortisone Injections

RISKS / SIDE EFFECTS INCLUDE:

- Bleeding
- Nerve damage
- Transient decrease in immunity
- High blood sugar
- Stomach ulcers
- Cataracts
- Increased risk of fracture
  (promotes deterioration of skeletal quality)

In a recent meta-analysis of 23 randomized trials involving more than 2000 patients, epidural steroid injections were compared with placebo for sciatica. **Injections produced small, statistically insignificant short-term improvement in leg pain and disability (but not less back pain) compared to the placebo.** This improvement was only over a short period – two weeks to three months, and beyond 12 months, there was no significant difference between groups.

This last complication is certainly not emphasized in clinical circles. Therapeutic steroids may reduce pain. However, using **steroid injections seems to promote deterioration of skeletal quality**, which is not surprising since other forms of steroid medication have long been associated with osteoporosis.

When the incidence of vertebral fractures was assessed, researchers discovered that an increasing number of injections was associated with an increased likelihood of fractures. **Each successive injection increased the risk of spinal fracture by 21%.**

This evidence exacerbates skeletal fragility and **promotes deterioration of skeletal quality**, similar to exogenous steroids, which is the leading cause of secondary osteoporosis. The rate of vertebral fracture following epidural steroid injections may be underestimated.

Based on systemic reviews, European and American guidelines conclude that epidural corticosteroid injections may temporarily relieve sciatica but **do not reduce the rate of subsequent surgery.**

The International® Disc Education Association

FDA

FDA Drug Safety Communication

FDA requires label changes to warn of rare but serious neurologic problems after epidural corticosteroid injections for pain

The FDA reviewed a sampling of cases from the FDA Adverse Event Reporting System (FAERS) database, as well as cases in the medical literature of serious neurologic adverse events associated with epidural corticosteroid injections. Serious adverse events included death, spinal cord infarction, paraplegia, quadriplegia, cortical blindness, stroke, seizures, nerve injury, and brain edema. Many cases were temporally associated with the corticosteroid injections, with adverse events occurring within minutes to 48 hours after the corticosteroid injections. In some cases, diagnoses of neurologic adverse events were confirmed through magnetic resonance imaging or computed tomography scan. Many patients did not recover from these reported adverse events

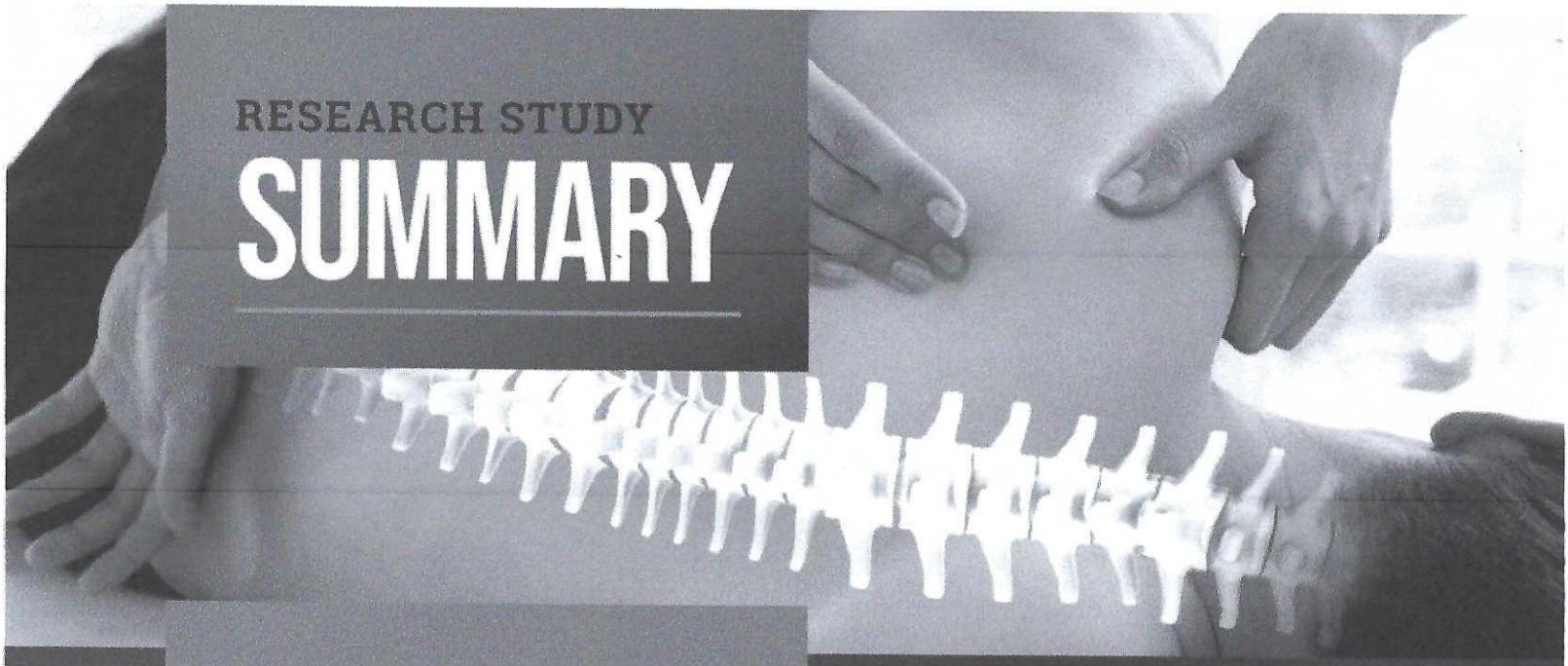
Rare but serious problems and neurologic events have occurred after injection of corticosteroids into the epidural space of the spine to treat neck and back pain, and radiating pain in the arms and legs.

These serious problems include loss of vision, paralysis, spinal cord infarction, paraplegia, quadriplegia, cortical blindness, stroke, and death.

These serious neurologic events have been reported with and without the use of fluoroscopy. The effectiveness and safety of injection of corticosteroids into the epidural space of the spine have not been established, and FDA has not approved corticosteroids for this use. Discuss the benefits and risks of epidural corticosteroid injections with your health care professional, along with the benefits and risks associated with other possible treatments..

Seek Emergency Medical Attention Immediately If You Experience

Loss of vision or vision changes; tingling in your arms or legs; sudden weakness or numbness of your face, arm, or leg on one or both sides of the body; dizziness; severe headache; or seizures.



RESEARCH STUDY

SUMMARY

Critically Evaluating the Evidence for Epidural Injections

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*Please see educational credits in study.

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SUMMARY:

Editorial discussion on the controversy over the efficacy of epidural steroid injections (ESIs) in treating chronic pain.

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OXFORD

EDITORIAL

Critically Evaluating the Evidence for Epidural Injections for Failed Back Surgery Syndrome: Should Pain Physicians Be Bracing for Impact?

Pain physicians and payers are on a collision course, and patients with chronic pain are along for the ride. As a confluence of factors makes treating chronic pain more challenging than ever, doctors and insurers are findings themselves at odds over the pay-for-service model. Reimbursement for commonly performed pain procedures has been decreasing [1], whereas the number of procedures performed per year has been steadily increasing [2]. Whether this is a cause-effect relationship, and if so, which phenomenon is the "cause," is unclear.

Unfortunately, the conflicting literature on injections does little to avert this collision. It is estimated that more than 9 million epidural steroid injections (ESIs) are performed annually in the United States [3], yet controversy still lingers regarding their efficacy. Evidence from randomized trials and recommendations from systematic reviews are disparate, with those performed by interventional pain practitioners being more likely to yield positive findings [4–7]; thus, many insurers have seized upon these negative studies as the rationale to decrease reimbursement, which may lead to even greater discrepancies in the interpretation of evidence. Some state legislatures have gone even further by limiting or eliminating coverage for ESIs in their state's Medicare and Medicaid programs [8]. The federal government has in some cases also followed suit, with the 2017 Veterans Administration/Department of Defense Clinical Practice Guideline for Diagnosis and Treatment of Low Back Pain providing a strong recommendation against the use of ESIs for chronic lumbar radiculopathy [9]. Consequently, the quest continues to find treatments that demonstrate superior benefit to ESI in well-designed studies, which would hopefully enable patients to continue to receive the treatments that many of them need to live happy and productive lives.

This issue of *Pain Medicine* contains a randomized controlled trial by Rapčan et al. [10] evaluating two different types of epidural lysis of adhesions (LOA): mechanical disruption vs mechanical disruption in addition to hyaluronidase and steroids. Adhesions and fibrosis in the epidural space are associated with a history of prior spine surgery or spinal stenosis and are thought to be a contributing factor to persistent pain related to those conditions [11,12]. The mechanism(s) by which epidural adhesions cause pain remains unclear, but likely involves both inflammatory and mechanical processes. However, the precise relationship between adhesions and pain is unknown. For example, three out of six studies that examined the relationship between pain and adhesions found no significant correlation [13]. Moreover, pain is the primary indication for spine surgery, and few patients experience complete eradication of pain after an operation. Because scarring is an inexorable consequence of surgery, nearly everyone who undergoes spine surgery will have both scar tissue and persistent pain. Therefore, determining whether scar tissue is a contributing factor to the pain, or whether persistent pain represents either residual pain or pain stemming from another etiology (e.g., nerve root injury, arachnoiditis, adjacent segment disease, recurrent herniation) that would not be amenable to adhesiolysis is paramount when selecting patients for a study that seeks to determine the effectiveness of epidural LOA. All of the randomized studies that evaluated LOA demonstrated improvement compared with conventional ESI, sham LOA, and alternative care, but only one was blinded, and all were underpowered and associated with other serious methodological shortcomings [13].

In the present trial, Rapčan and colleagues compared the effects of purely mechanical LOA with combined mechanical-chemical LOA in patients with failed back surgery syndrome (FBSS). The authors reviewed the theory and history of epidural LOA, the mechanism(s) by which adhesions likely cause pain, and the rationale for performance of LOA. Both of the treatment groups underwent epiduroscopy, injection of local anesthetic, and mechanical LOA via either laser, balloon inflation, or radiofrequency, but the second group also received targeted injections of corticosteroid and hyaluronidase. Statistically significant improvements were shown in both groups in terms of function, back pain, and leg pain at six-month follow-up. The major between-group difference was the statistically significant persistence of back pain relief at 12 months in the group that received steroid and hyaluronidase, with the difference for leg pain falling shy of statistical significance. Overall, these results are encouraging given the improvements in all outcome measures among both groups through six months, but they raise more questions than they answer.

Just how reliable are these findings? Studies that compare two different therapeutic treatments should

theoretically require many more patients to detect a difference between groups than those comparing a treatment with placebo. Both the US Food and Drug Administration and the Department of Health and Human Services have determined that a sample size of about 400 patients is necessary to detect a difference between epidural steroids and placebo injections in well-selected patients [4,14]. In a study evaluating a treatment for failed back surgery syndrome, which tends to respond more poorly to epidural injections than herniated discs [6], the number would be even higher. Yet, Rapčan et al. enrolled only 45 people in both groups. For a *P* value greater than 0.01 in the context of wide confidence intervals in a study that enrolls fewer than 50 individuals, the chances of these results being reproducible are exponentially less than in a more methodologically sound study. A second question surrounds the pharmacological basis for persistent relief lasting one year, when the effects of steroids—the main difference between the groups, as the added value of hyaluronidase is at best controversial [15]—do not last longer than three months [6]. Last, the authors found a significant difference for back pain, but not leg pain, which tends to respond better to epidural injections. These issues raise the question of whether the small difference detected is real and replicable or a statistical anomaly.

So how do we proceed from here? The search for effective and appropriately researched pain interventions must continue. As regulatory and legislative bodies increasingly exert their influence on the practice of pain management, it is incumbent on pain physicians to advocate for our patients via the promotion and propagation of sound research. However, as with almost everything in medicine, this is easier said than done. In addition to the technical and practical challenges of rigorously evaluating chronic pain interventions, such as the difficulties in blinding and ethics of sham procedures for high-risk interventions (e.g., stopping anticoagulation, penetrating and injecting inert substances into the neuraxis), an additional barrier to conducting these trials is the substantial costs, which are unlikely to be borne by a pharmaceutical or device company with no proprietary interest, or if history is any indicator of future behavior, the federal government.

Concomitant to the conduct of relevant and methodologically sound research is the need to "police" our specialty. This includes both instituting and supporting regulatory measures such as limiting the overuse of procedures, which attracts scrutiny and adversely affects the risk:benefit ratio, and critically evaluating the published literature. The study by Rapčan asks an important question, and though the findings are intriguing, they are by no means definitive. Future research should employ large-scale, well-designed studies to determine efficacy, identify which patients are most likely to benefit from epidural LOA, and establish what the optimum treatment regimen is. If we are not able to regulate our own specialty, then we must be prepared for outsiders to step in and fill the gap.

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References

1 Manchikanti L, Kaye A, Hirsch J. Proposed medicare physician payment schedule for 2017: Impact on inteventional pain management practices. Pain Physician 2016;19:E935–55.

2 Manchikanti L, Pampati V, Falco F, Hirsch J. An updated assessment of interventional pain management techniques in the medicare population: 2000–2013. Pain Physician 2015;18:E115–27.

3 Cohen S, Furman M, Weber N, Singh J. Single versus two-level transforaminal epidural steroid injection for treating lumbosacral radicular pain: What is the evidence? PM R 2015;7(8):883–8.

4 Friedly J, Comstock B, Turner J, et al. A randomized trial of epidural glucocorticoid injections for spinal stenosis. N Engl J Med 2014;371(1):11–21.

5 Bhatia A, Flamer D, Shah P, Cohen S. Transforaminal epidural steroid injections for treating lumbosacral radicular pain from herniated intervertebral discs: A systematic review and meta-analysis. Anesth Analg 2016;122(3):857–70.

6 Cohen S, Bicket M, Jamison D, et al. Epidural steroids: A comprehensive, evidence-based review. Reg Anesth Pain Med 2013;38(3):175–200.

7 Cohen SP, Hayek S, Semenov Y, et al. Epidural steroid injections, conservative treatment, or combination treatment for cervical pain: A multicenter, randomized, comparative-effectiveness study. Anesthesiology 2014;121(5):1045–55.

8 Oregon State Health Evidence Review Commission. Oregon State Health Evidence Review Commission coverage guidance: Low back pain – corticosteroid injections. Available at: http://www.oregon.gov/oha/HPA/CSI-HERC/EvidenceBasedReports/Coverage

%20Guidance%20-%20Low%20back%20pain-Corticosteroid%20Injections.pdf (accessed April 2018).

9 VA/DoD. VA/DoD clinical practice guideline for diagnosis and treatment of low back pain, version 2.0–2017. Available at: https://www.healthquality.va.gov/guidelines/Pain/lbp/VADoDLBPCPG092917.pdf (accessed April 2018).

10 Rapčan R, Kočan L, Mláka J, et al. A randomized, multicentre, double-blinded, parallel, pilot study, assessing the effect of mechanical adhesiolysis versus adhesiolysis with corticosteroid and hyaluronidase administration into the epidural space during epiduroscopy. Pain Med 2018;19(7):1436–44.

11 Kuslich S, Ulstrom C, Michael C. The tissue origin of low back pain and sciatica: A report of pain response to tissue stimulation during operations on the lumbar spine using local anesthesia. Orthop Clin North Am 1991;22(2):181–7.

12 Ross J, Robertson J, Frederickson R, et al. Association between peridural scar and recurrent radicular pain after lumbar discectomy: Magnetic resonance evaluation. ADCON-L European Study Group. Neurosurgery 1996;38(4):855–61.

13 Jamison D, Hsu E, Cohen S. Epidural adhesiolysis: An evidence-based review. J Neurosurg Sci 2014; 58(2):65–76.

14 Semnur Pharamceuticals, Inc. Corticosteroid lumbar epidural analgesia for radiculopathy. Available at: https://clinicaltrials.gov/ct2/show/NCT03372161 (accessed April 2018).

15 Lee F, Jamison D, Hurley R, Cohen S. Epidural lysis of adhesions. Korean J Pain 2014;27(1):3–15.