Pain Medicine 2010; 11: 1141–1143
Wiley Periodicals, Inc.

# EDITORIALS

# Demystifying Lumbar Transforaminal Epidural Steroids: A Seminal Efficacy Study of a Specific Spinal Injection

Medical research and health care delivery is in a state of transition—and uncertainty. The initial disquiet following the introduction of evidence-based decision making almost two decades ago [1,2] has given rise to a more profound angst as researchers, health care analysts, and insurers all struggle with the imperative of defining which treatments are simultaneously efficacious, effective, *and* efficient. Vaguely defined terms such as health utility indices, together with a dazzling array of initialisms—ICER (incremental cost-effectiveness ratio), HRQoL (health-related quality-of-life), SCB (substantial clinical benefit), and CEACs (cost-effectiveness acceptability curves)—leave most of us numb. Meanwhile, the cry for evidence grows louder.

Traditionally, placebo randomized controlled trials (P-RCTs) have been held as the gold standard for determining if a particular treatment is *efficacious*. However, by necessity, placebo controlled trials often involve short-term follow-up, and are costly and difficult to perform, particularly with invasive treatments. RCTs are also criticized as representing an idealized patient population—one that is rarely, if ever, seen in routine clinical practice.

On the other hand, despite being currently fashionable, comparative effectiveness research (CER) is far from ideal. Comparative effectiveness research attempts to prove whether or not a particular treatment is *effective* in the "real world." But CER is heterogeneous, running the spectrum from data mining of existing databases (Medicare, Ingenix, and others) to observational studies to formal registries. The most legitimate method involves using large registries; however, collecting registry data is particularly difficult and expensive, and the resulting datasets are often incomplete [3].

Most recently, the concept of *value* in spine care has been touted [4–6]. Commonly defined as quality/cost, value attempts to go beyond mere proof of efficacy and effectiveness, to examine the *efficiency* of a treatment. Despite being discussed for decades, this field is still in its infancy, with many concepts requiring validation and refinement. Nagging questions remain about patient willingness to accept health care "rationing" resulting from quality adjusted life years (QALYs) [7] or other metrics, and distinctions are being drawn about which aspects of value are most important: the intrinsic value of a particular treatment, the value to a patient, or the value to society as a whole. Very quickly, the argument shifts from science to economics, and even to philosophy. It is in this context that we examine the extraordinary placebo controlled RCT of transforaminal steroid injection by Bogduk et al. [8]

By any measure, a five-arm P-RCT is a tremendous accomplishment. It is unparalleled in the world of spine treatments. Despite the complexity of the study design, the authors have presented the results in a refreshingly straightforward manner. Their conclusions are cogent: "In essence, transforaminal injection of steroids is a viable alternative to surgery for lumbar radicular pain due to disc herniation. Its immediate yield is modest, but substantial, and is not simply a placebo effect. For long-term efficacy, proof beyond reasonable doubt would require prohibitively large studies." Yet, the succinct presentation of the results belies a deeper and subtler meaning that is translatable across all spine treatments.

At its most basic, the study is an effort to determine whether the route of administration or the agent delivered is important to the effectiveness of transforaminal injection of steroids (TFST) for lumbar radicular pain from a disc herniation. This involved randomizing patients into one of five groups: TFST, intramuscular injection of steroids (IMST), transforaminal injection of local anesthetic, transforaminal injection of normal saline (TFNS), or intramuscular injection of normal saline. The primary outcome measure was the proportion of patients who achieved ≥50% relief of pain at 1 month after treatment. Secondary outcomes included measures of function, disability, use of other health care, duration of relief beyond 1 month, and patient-specified functional outcomes.

The results are clear: 54% of the active group achieved success at 1 month, and 25% sustained relief for over 12 months. This is particularly impressive given the stringent study design, which included a requirement for ≥50% pain reduction, well beyond the minimal clinically important difference in visual analog pain score of 1.6/10 recently cited in the literature [9]. Patients were also able to opt out of the study and thus counted as failures, if they had not responded within 1 week—a shorter time frame than many accord for the maximal therapeutic effect from steroid treatment. Additionally, chronic patients were included in the study. In fact, the median duration of pain

in the TFST chronic cohort was 96 weeks. The patients were also in moderate to severe distress, as reflected by a positive straight leg raise at <30°; median visual analog leg pain scores of 7–8/10; and moderately to severely disabled ratings on SF-36 physical functioning and social functioning subscales, and the Roland–Morris instrument. Although this effectively separated patients with the less common radicular pain from patients with the more common somatic referred pain, it also preferentially selected a group of patients who were more disabled. One can only wonder what the success rates would have been in a less disabled, more acute/subacute cohort that was assessed over a longer time frame.

So, what can we learn from this study? One of the chief lessons is that analysis of categorical results is essential when the data is not evenly distributed. Examining an entire treatment group using mean values can obscure a valid treatment effect in a subset. Indeed, in the Bogduk study, using standard analyses and obtaining the mean improvement in each group, TFST would be no more effective than TFNS at 1 month, with a *P* value of 0.071. In reality, there was not a normal distribution of values. The results were bimodal: patients either responded to transforaminal steroid injection or they did not. The upshot is that TFST are superior to all other cohorts at 1 month when selecting for patients that achieved ≥50% pain relief. This may potentially explain the negative results of prior studies on transforaminal steroid injection that used mean values and not categorical data [10–13].

This also highlights a goal for future research: to better determine which patients respond to any given treatment. Indeed, this is the crux of the issue facing all of spine care. As Mant stated, "The paradox of the clinical trial is that it is the best way to assess whether an intervention works, but is arguably the worst way to assess who will benefit from it" [14]. That, however, was not the aim of the Bogduk study.

More vexing questions concern how and when to apply treatments which confer a significant improvement in pain and function, but which are short lived. To truly appreciate whether or not a treatment is effective, one must study patients longitudinally over long periods of time. One must also allow repeated treatments for therapies with shorter durations of effect. When compared with surgery, analysis of non-operative care over a 2-year period revealed only a modest benefit in QALYs in favor of surgery (mean 1.64 vs 1.44), but at a significantly higher cost. The mean total direct and indirect surgical costs were $27,273, vs non-operative costs of $13,135 over the 2-year period [15]. The ICER (cost per QALY) gained for surgical treatment relative to non-operative care in the general population was $69,403, not insignificant in terms of cost per incremental benefit.

Bogduk, however, chose to use a different measure of treatment effect, the number needed to treat (NNT). As first described by Cook and Sackett in 1995, the NNT cannot only be used to directly compare costs between two treatments, it can also easily be modified to extrapolate differences in patient baseline variables [16]. Perhaps most importantly, it is clinically intuitive. From Bogduk's analysis, one can easily grasp that every third patient will be significantly improved beyond what an IMST or a TFNS can offer. More to the point, one can observe that one in four patients will retain significant benefit with TFST at 12 months, while avoiding the cost of surgery.

In the end, this landmark study has vindicated transforaminal steroid injection for lumbar radicular pain as superior to placebo. Further studies are now needed to determine the durability of the effect of repeated injections over time, to compare that with the long-term utility of other treatments (including surgery), and to determine which patients are most likely to benefit from treatment. Studies are also needed to better assess the indirect value of transforaminal injections with respect to maintaining a patient's ability to work and reducing usage of other health care services. We might find what many of us have suspected all along: Transforaminal steroid injections significantly benefit patients by allowing them to continue to function with less pain while they are improving according to the natural history of the process. For many, this is sufficient to prevent the need for surgery.

RAY BAKER, MD
*12301 NE 10th Place, Suite 101*
*Bellevue, Washington, USA*

**References**

1 Evidence-based Medicine Working Group. Evidence-based medicine. A new approach to the teaching of medicine. JAMA 1992;268:2420–5.

2 Sackett DL, Haynes RB, Guyatt GH, Tugwell P. Clinical Epidemiology: A Basic Science for Clinical Medicine, 2nd edition. Boston, MA: Little Brown; 1991.

3 Roder C, Staub L, Dietrich D, et al. Benchmarking with Spine Tango: Potentials and pitfalls. Eur Spine J 2009;18(suppl 3):S305–11.

4 Rihn JA, Berven S, Allen T, et al. Defining value in spine care. Am J Med Qual 2009;24(suppl 6):4S–14S.

5 Hatten AL, Gatchel RJ, Polatin PB, Stowell AW. A cost-utility analysis of chronic spinal pain treatment outcomes: Converting SF-36 data into quality-adjusted life years. Clin J Pain 2006;22(8):700–11.

6 Hansson E, Hansson T. The cost-utility of lumbar disc herniation surgery. Eur Spine J 2007;16:329–37.

7 Neumann PJ, Greenberg D. Is the United States ready for QALYs? Health Aff (Millwood) 2009;28(5):1366–71.

8 Bogduk N, et al. The efficacy of transforaminal injection of steroids for the treatment of lumbar radicular pain. Pain Med 2010;11:1149–68.

9 Copay AG, Glassman SD, Subach BR, et al. The minimum clinically important difference in lumbar spine surgery patients. A choice of methods using the Oswestry Disability Index, MOS Short Form 36, and pain scales. Spine J 2008;8:968–74.

10 Karppinen J, Malmivaara A, Kurunlahti M, et al. Periradicular infiltration for sciatica. A randomized controlled trial. Spine 2001;26:1059–67.

11 Karppinen J, Ohinmaa A, Malmivaara A, et al. Cost-effectiveness of periradicular infiltration for sciatica. Subgroup analysis of a randomized controlled trial. Spine 2001;26:2587–95.

12 Ng L, Chaudhary N, Sell P. The efficacy of corticosteroids in periradicular infiltration for chronic radicular pain. Spine 2005;30:857–62.

13 Tafazal S, Ng L, Chaudhary N, Sell P. Corticosteroids in periradicular infiltration for radicular pain: A randomised double blind controlled trial. One year results and subgroup analysis. Eur Spine J 2009;18:1220–5.

14 Mant D. Can randomised trials inform clinical decisions about individual patients? Lancet 1999;353: 743–6.

15 Tosteson AN, Skinner JS, Tosteson TD, et al. The cost-effectiveness of surgical versus nonoperative treatment for lumbar disc herniation over two years: Evidence from the Spine Patient Outcomes Research Trial (SPORT). Spine 2008;33:2108–15.

16 Cook RJ, Sackett DL. The number needed to treat: A clinically useful measure of treatment effect. BMJ 1995;310(6977):452–4.