

**Letters to the Editor**

## **The Food and Drug Administration's Recent Action on April 23, 2014 Failed to Appropriately Address Safety Concerns about Epidural Steroid Use**

### **TO THE EDITOR:**

As patient safety advocates, we are thankful for the oversight of the US Food and Drug Administration (FDA) in our health care system. Unfortunately, it is our belief that recent actions of the FDA were incorrect and could adversely impact thousands of Americans who suffer from chronic pain. This is increasingly troubling in a period of time when we seek treatment methods that can reduce the need for addictive and often dangerous medication choices. On April 23, 2014 the FDA warned that the injection of corticosteroids into the epidural space of the spine "may result in rare but serious adverse events, including loss of vision, stroke, paralysis and death" (1). Furthermore, they required the addition of a warning to the drug labels of injectable corticosteroids to describe these risks. They further state that the "effectiveness and safety of the drugs for this use have not been established, and the FDA has not approved corticosteroids for such use" (1). While the FDA has not approved the use of epidural steroids to manage spinal pain conditions, these injections have been used to treat radicular type pain since at least 1960 and have been safely administered to millions of patients worldwide (2).

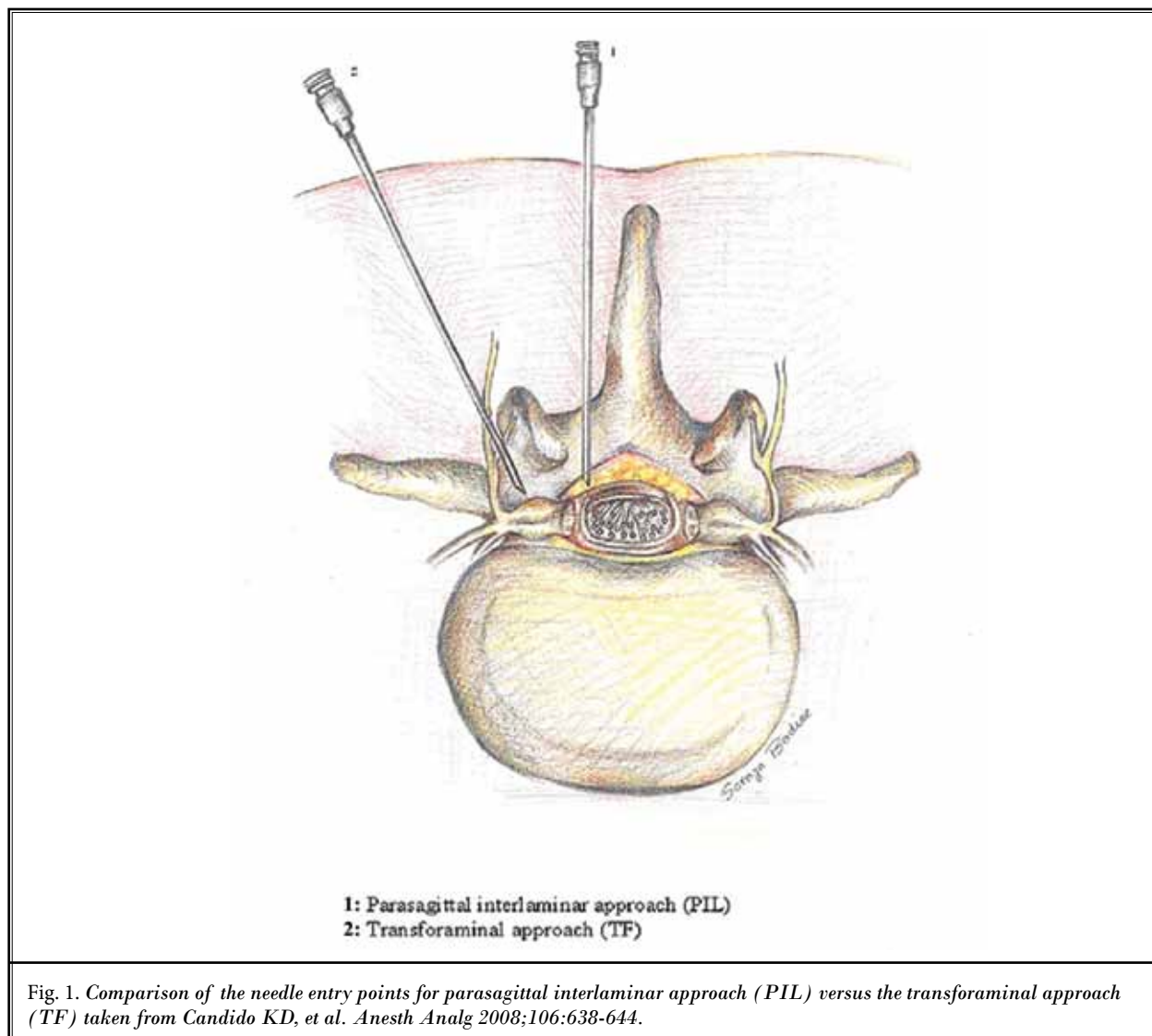
We believe that the FDA has misspoken with this warning, to the detriment of clinicians and patients alike. Their document contains 17 references supporting their stance. Of these 17 references, 11 are exclusively concerned with the administration of steroids using a transforaminal approach to the spine, which is decidedly distinct and separate from a classic interlaminar administration of these drugs (3). In fact, none of the remaining 6 references deals with complications associated with lumbar interlaminar epidural steroid injections at all, which is why the message being conveyed by that organization will lead to confusion and dissemination of misinformation between and among clinicians and patients. The FDA does not rely upon evidence-based medicine in formulating this warning,

but instead has used isolated case reports, which does not amount to a critical appraisal of evidence either for efficacy of these techniques, or for potential complications. The scientific-minded must ask if it is appropriate that the FDA demand rigorous, peer-reviewed and evidenced-based studies in making its own determinations as to the appropriateness of any given therapeutic modality, while they rely upon documentation that could not possibly withstand their own scrutiny if used in support of a given treatment modality.

Finally, the FDA's use of reference #17 is the most interesting, since that is a review article that states, "The data are reassuring and suggest that central neuraxial (i.e., epidural and spinal) block has a low incidence of major complications, many of which resolve within 6 months" (4).

While we concur with the FDA in providing warnings regarding transforaminal neuraxial steroid injections, particularly in the cervical spine, the same risks (spinal infarction, paralysis, death) are very rarely associated with lumbar interlaminar injections, and lumping all corticosteroid injections into the same category is not appropriate and is technically incorrect. Transforaminal injections of corticosteroids are not synonymous with interlaminar epidural steroid injections (Fig. 1). Additional unique risks of the transforaminal approach include an increased risk of intradiscal injection (5). The FDA did not distinguish the use of various modalities such as nonparticulate steroids used for transforaminal injections versus particulate steroids. Based on the data, this is unwise if attempting to give a useful safety guide to interested parties. In point of fact, there is no case report in the medical literature of paralysis or death due to spinal infarction that has been unequivocally associated with the use of these nonparticulates.

The FDA should amend its language to reflect the proper use of its own references, or prepare a new statement that factually outlines the risks and differ-



References used in the FDA letter	Type of Article	Number of Patients	Approach	Type of Steroids	Imaging guidance
1. Rathmell JP. Toward improving the safety of transforaminal injection. <i>Anesth Analg</i> 2009;109:8-10	Editorial	N/A	Transforaminal		
2. Kennedy DJ, Dreyfuss P, Aprill CN, Bogduk N. Paraplegia following image-guided transforaminal lumbar spine epidural steroid injection: two case reports. <i>Pain Med</i> 2009;10:1389-94.	Case Reports	1 1	Lumbar Transforaminal	6 mg betamethasone + 1 ml 0.75% bupivacaine 160 mg methylprednisolone + 6 ml 0.375% bupivacaine	Fluoroscopy  CT
3. Windsor RE, Storm S, Sugar R, Nagula D. Cervical transforaminal injection: review of the literature, complications, and a suggested technique. <i>Pain Physician</i> 2003;6:457-465.	Systematic Review and 3 case reports	N/A	Cervical Transforaminal	6 mg betamethasone + 2.5 mL of 0.75% bupivacaine (1 patient) or betamethasone = 2 mL lidocaine (1 patient) both partially injected	Fluoroscopy

References used in the FDA letter	Type of Article	Number of Patients	Approach	Type of Steroids	Imaging guidance
4. Beckman WA, Mendez RJ, Paine GF, Mazzilli MA. Cerebellar herniation after cervical transforaminal epidural injection. <i>Reg Anesth Pain Med</i> 2006;31:282-5.	Case Report	1	Cervical Transforaminal	60 mg methylprednisolone + 0.75 ml 1% lidocaine	Fluoroscopy
5. Ludwig MA, Burns SP. Spinal cord infarction following cervical transforaminal epidural injection: a case report. <i>Spine</i> 2005;30:E266-8.	Case Report	1	Cervical Transforaminal	0.75 ml triamcinolone + 0.75 ml 0.75% bupivacaine	Fluoroscopy
6. Somayaji HS, Saifuddin A, Casey AT, Briggs TW. Spinal cord infarction following therapeutic computed tomography-guided left L2 nerve root injection. <i>Spine</i> 2005;30:E106-8.	Case Report	1	Lumbar Nerve root injection (Transforaminal)	40 mg triamcinolone + 1 ml 0.5% bupivacaine	CT
7. Tripathi M, Nath SS, Gupta RK. Paraplegia after intracord injection during attempted epidural steroid injection in an awake-patient. <i>Anesth Analg</i> 2005;101:1209-11. Thoracic ILESII	Case Report	1	Thoracic Interlaminar	40 mg triamcinolone + 10 ml 0.125% bupivacaine	Fluoroscopy
8. Bose B. Quadripareisis following cervical epidural steroid injections: case report and review of the literature. <i>Spine J</i> 2005;5:558-63.	Case Report	1	Cervical Inter-laminar	80 mg methylprednisolone acetate	Fluoroscopy (no flims?)
9. Tiso RL, Cutler T, Catania JA, Whalen K. Adverse central nervous system sequelae after selective transforaminal block: the role of corticosteroids. <i>Spine J</i> 2004;4:468-74.	Case Report	1	Cervical Transforaminal	80 mg triamcinolone + 2 ml 0.25% bupivacaine	Fluoroscopy
10. Edlow BL, Wainger BJ, Frosch MP, Copen WA, Rathmell JP, Rost NS. Posterior circulation stroke after C1-C2 intraarticular facet steroid injection: evidence for diffuse microvascular injury. <i>Anesthesiology</i> 2010;112:1532-5.	Case Report	1	Cervical Facet Joint Injection	80 mg triamcinolone	None
11. Meyer HJ, Monticelli F, Kiesslich J. Fatal embolism of the anterior spinal artery after local cervical analgetic infiltration. <i>Forensic Sci Int</i> 2005;149:115-9.	Case Report	1	Cervical Paravertebral Injection	5 ml cortisone and xylocaine	None
12. Suresh S, Berman J, Connell DA. Cerebellar and brainstem infarction as a complication of CT-guided transforaminal cervical nerve root block. <i>Skeletal Radiol</i> 2007;36:449-52.	Case Report	1	Cervical Transforaminal	40 mg triamcinolone	CT
13. Deshpande DM, Krishnan C, Kerr DA. Transverse myelitis after lumbar steroid injection in a patient with Behcet's disease. <i>Spinal Cord</i> 2005;43:735-7. "left L2 nerve root" injection	Case Report	1	Lumbar Nerve root injection (Transforaminal)	6 mg betamethasone + 1 ml 0.5% bupivacaine/epinephrine	
14. Lyders EM1, Morris PP. A case of spinal cord infarction following lumbar transforaminal epidural steroid injection: MR imaging and angiographic findings. <i>AJNR Am J Neuroradiol</i> 2009;30:1691-3.	Case Report	1	Lumbar Transforaminal	1 ml triamcinolone + 0.25% bupivacaine	Fluoroscopy
15. Popescu A, Lu A, Gardner K. An unusual mechanism for spinal cord infarction – case report. <i>Ann Neurol</i> 2007;62(Suppl 11):32	Conference Abstract Case Report	1	Cervical Transforaminal	methylprednisolone	Fluoroscopy
16. Ziai WC1, Ardelt AA, Llinas RH. Brainstem stroke following uncomplicated cervical epidural steroid injection. <i>Arch Neurol</i> 2006;63:1643-6.	Case Report	1	Cervical Inter-laminar	40 mg methylprednisoloneacetate	
17. Cook TM, Counsell D, Wildsmith JA; Royal College of Anaesthetists Third National Audit Project. Major complications of central neuraxial block: report on the Third National Audit Project of the Royal College of Anaesthetists. <i>Br J Anaesth</i> 2009;102:179-90.	Review	N/A			

entiate the respective approaches to spinal injections using steroid medications, while also accounting for the differences in medication type and the presence or absence of particulate matter in those injectates. From a safety perspective, patients and clinicians alike should be presented with factual and evidence-based assessments of treatment modalities to avoid causing unnecessary panic and to eliminate the dissemination of misinformation regarding treatment options available to them. Access to effective and safe treatment is an underlying premise of the evolving health care environment, and we propose an immediate retraction of the April 23, 2014 FDA warning regarding epidural steroid use since this warning does not accomplish that mission.

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## REFERENCES

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2. Brown JH. Pressure caudal anesthesia and back manipulation. Conservative method for treatment of sciatica. *Northwest Med* 1960; 59:905-909.
3. Candido KD, Rana MV, Sauer R, Chupatanakul L, Tharian A, Vasic V, Knezevic N. Concordant Pressure paresthesia during interlaminar lumbar epidural steroid injections correlates with pain relief in patients with unilateral radicular pain. *Pain Physician* 2013; 16:497-511.
4. Cook TM, Counsell D, Wildsmith JA; Royal College of Anaesthetists Third National Audit Project. Major complications of central neuraxial block: Report on the Third National Audit Project of the Royal College of Anaesthetists. *Br J Anaesth* 2009; 102:179-190.
5. Candido KD, Katz J, Chinthagada M, McCarthy RA and Knezevic N. Incidence of intradiscal injection during lumbar fluoroscopically-guided transforaminal and interlaminar epidural steroid injections. *Anesth Analg* 2010; 110:1464-1467.