

Epidural Steroid Injections and the Risk of Serious Neurologic Adverse Reactions

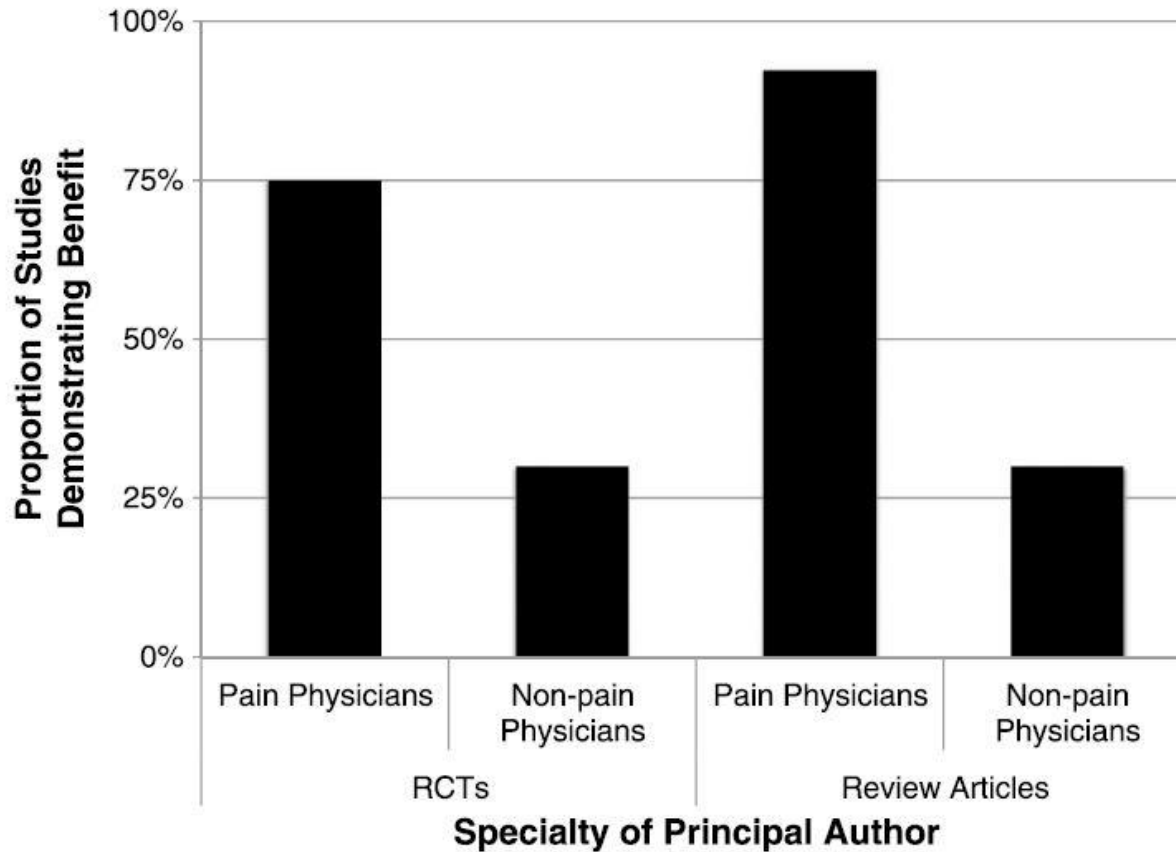
Testimony by Sarah Sorscher, JD/MPH
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before the FDA's Anesthetic and Analgesic Drug Products Advisory
Committee
November 24, 2014

Weak Evidence of Efficacy

- Limitations of published research
 - limited protocol descriptions, limited data on protocol deviations, lack of original datasets, lack of ability to inspect sites to verify data and conduct.
- Lack of consistency and replicability
 - “findings are often mixed and comparisons are difficult to make due to differences in trial designs”¹
- Potential Bias

¹ FDA Briefing Document, Anesthetic and Analgesic Drug Products Advisory Committee Meeting, November 24-25, 2014 (page 20).

Influence of Medical Specialty on Study Findings



Source: Cohen SP, Bicket MC, Jamison D, Wilkinson I, Rathmell JP, Epidural steroids: a comprehensive, evidence-based review. *Reg Anesth Pain Med* 2013;38:175-200.

Small Clinical Benefit

Table 2. Summary of Outcomes and Quality of Outcome Assessment

Studies (References), by Outcome	Quality Assessment			Patients, n		Effect*		Quality	Importance
	Risk of Bias	Inconsistency	Imprecision	Reporting Bias	Corticosteroid Group	Placebo Group	WMD† (95% CI)		
Leg pain (0–100 scale)									
Short-term follow-up 14 trials (37–40, 43–47, 50, 51, 59, 61)	No serious risk‡	No serious inconsistency§	No serious imprecision	Undetected¶	664	652	-6.2 (-9.4 to -3.0)	High	Important**
Long-term follow-up 7 trials (37, 38, 45, 46, 50, 51, 60)	No serious risk‡	No serious inconsistency§	No serious imprecision	Undetected¶	364	350	-4.8 (-10.2 to 0.7)	High	Important**
Back pain (0–100 scale)									
Short-term follow-up 6 trials (37, 40, 45, 46, 53, 59)	No serious risk‡	No serious inconsistency§	No serious imprecision	Undetected¶	370	353	0.5 (-3.9 to 4.8)	High	Important**
Long-term follow-up 3 trials (37, 45, 46)	No serious risk‡	No serious inconsistency§	No serious imprecision	Undetected¶	232	221	3.4 (-2.4 to 9.2)	High	Important**
Disability (0–100 scale)									
Short-term follow-up 10 trials (37, 39, 40, 45, 46, 50, 51, 53, 59, 61)	No serious risk‡	No serious inconsistency§	No serious imprecision	Undetected¶	585	569	-3.1 (-5.0 to -1.2)	High	Important**
Long-term follow-up 6 trials (37, 45, 46, 50, 51, 60)	No serious risk‡	No serious inconsistency§	No serious imprecision	Undetected¶	352	339	-2.7 (-6.8 to 1.3)	High	Important**

* Negative values favor the epidural corticosteroid group
WMD = weighted mean difference on 0 to 100 point scale

Source: Pinto RZ, Maher CG, Ferreira ML, et al. Epidural corticosteroid injections in the management of sciatica: A systematic review and meta-analysis. *Ann Intern Med* 2012;157:865-877.

Catastrophic Injuries

- Death
- Paralysis
- Stroke
- Blindness
- Seizures
- Bowel and bladder dysfunction
- Behavioral changes
- Arachnoiditis

Mitigation Strategies

- Use of “non-particulate steroids”
- Imaging
- “Safer” routes of administration
- Blunted needle

None of these strategies appears to eliminate the risk of catastrophic injury.

Mitigation Strategies

- Use of “non-particulate steroids”
 - Class-wide adverse events²
 - Hemorrhagic brain injury with particulate and non-particulate methylpredisolone³

² FDA Briefing Document, Anesthetic and Analgesic Drug Products Advisory Committee Meeting, November 24-25, 2014 (page 52).

³ Dawley JD, Moeller-Bertram T, Wallace MS, Patel P. Intra-arterial injection in the rat brain: Evaluation of steroids used for transforaminal epidurals. *Spine* 2009;34:1638-1643.

Mitigation Strategies

- Imaging
 - Rate of intravascular injection approaching 20% despite the use of fluoroscopy⁴
 - FAERS analysis:⁵ 33 serious neurologic adverse events involved imaging (including with contrast agent, fluoroscopy, computed tomography, and angiography)

⁴ Popescu A, Lai D, Lu A, Gardner K, Stroke following epidural injections—case report and review of the literature. *J Neuroimaging* 2013;23:118-121.

⁵ FDA Briefing Document, Anesthetic and Analgesic Drug Products Advisory Committee Meeting, November 24-25, 2014 (page 84).

Mitigation Strategies

Potential risk of vascular penetration and serious injury remains present with:

- All routes of administration (transforaminal, interlaminar, and caudal)
- Blunted needle

Requested Actions

Epidural steroid injections offer dubious benefits and present risks of life-threatening and disabling harm that cannot be eliminated through currently proposed mitigation strategies.

We request, on all injectable steroid products:

- A boxed warning
- A contraindication against epidural injection