FDA Hearing on EpiduralSteroid Injections

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The FDA's mission (in simple terms):

• To promote and protect the public health by helping safe and effective products reach the market in a timely way.

• To monitor products for continued safety after they are in use.

• To help the public get the accurate, science-based information needed to improve health.
The FDA had to balance the dangers posed by opioids against "the very real medical needs of the estimated 100 million Americans living with chronic pain or coping with pain at the end of life, which is also a major public health problem in this country."

FDA Commissioner Margaret Hamburg, MD statement

(Drug Abuse Summit in Atlanta, Georgia, in April 2014)
# Complications of Chronic Pain Therapy

<table>
<thead>
<tr>
<th>Modalities</th>
<th>Deaths (Fatalities)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DRUGS</strong></td>
<td></td>
</tr>
<tr>
<td>Tylenol</td>
<td>1,000   (2013)</td>
</tr>
<tr>
<td>NSAIDS</td>
<td>17,000  (Per year)</td>
</tr>
<tr>
<td>Opioids (Source: CDC)</td>
<td>16,917  (2011)</td>
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<tr>
<td>Methadone alone – subcategory under opioids (Source: CDC)</td>
<td>4,418   (2011)</td>
</tr>
<tr>
<td>Spinal fusions &amp; Laminectomy*</td>
<td>1,286   (2008)</td>
</tr>
<tr>
<td>INTERVENTIONAL Techniques (total)</td>
<td>(131)   (10-20 years)</td>
</tr>
<tr>
<td>Arachnoiditis</td>
<td>(41)</td>
</tr>
<tr>
<td>Particulate steroids</td>
<td>(116)</td>
</tr>
<tr>
<td>Non-particulate (only 2% use NP)</td>
<td>(4)</td>
</tr>
</tbody>
</table>

Multistate Outbreak of Fungal Meningitis not included with 751 Cases and 64 Deaths

Numbers if ( ) indicates Fatalities

Safety Announcement

[4-23-2014] The U.S. Food and Drug Administration (FDA) is warning that 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.

Efficacy:
The effectiveness and safety of the drugs for this use have not been established, and FDA has not approved corticosteroids for such use.
Epidural steroid injections safety recommendations approved by the Multi-Society Pain Workgroup (MPW)

1. Cervical interlaminar (IL) ESI are associated with a rare risk of catastrophic neurologic injury.
2. Transforaminal (TF) ESI using particulate steroid is associated with a rare risk of catastrophic neurovascular complications.
3. All cervical interlaminar (IL) epidural steroid injections should be performed using image-guidance, with appropriate AP, lateral or contralateral oblique views, and a test-dose of contrast medium.
4. Cervical transforaminal ESIs should be performed by injecting contrast medium under real-time fluoroscopy and/or DSA, in a frontal plane, before injecting any substance that may be hazardous to the patient.
5. Cervical interlaminar epidural steroid injections are recommended to be performed at C7-T1, but preferably not higher than the C6-C7 level.
6. No cervical interlaminar epidural steroid injection should be undertaken, at any segmental level, without reviewing, before the procedure, prior imaging studies that show there is adequate epidural space for needle placement at the target level.
7. Particulate steroids should not be used in cervical TF injections.
8. All lumbar IL ESI should be performed using image-guidance, with appropriate AP, lateral or contralateral oblique views, and a test-dose of contrast medium.
9. Lumbar TF ESIs should be performed by injecting contrast medium under real-time fluoroscopy and/or DSA, in a frontal plane, before injecting any substance that may be hazardous to the patient.
10. A non-particulate steroid (e.g. dexamethasone) should be used for the Initial injection in lumbar transforaminal epidural injections.
11. There are situations where particulate steroids could be used in the performance of lumbar TF ESIs.
12. Extension tubing is recommended for all TF ESIs.
13. A face mask and sterile gloves must be worn during the procedure.
14. The ultimate choice of what approach or technique (IL vs. TF ESI) to use should be made by the treating physician by balancing potential risks vs. benefits with each technique for each given patient.
15. Cervical and lumbar IL-ESIs can be performed without contrast in patients with documented contra-indication to use of contrast (e.g. significant history of contrast allergy or anaphylactic reaction).
16. TF ESIs can be performed without contrast in patients with documented contraindication to use of but in these circumstances, particulate steroids are contraindicated and only preservative free, particulate free steroids should be used.
17. Moderate to heavy sedation is not recommended for epidural steroid injections, but if light sedation is employed, the patient should remain able to communicate pain or other adverse sensations or events.

ESI = epidural steroid injection; AP = anteroposterior; DSA = digital subtraction angiography
• ASIPP submitted
  o  Comment letter
  o  Letter with 1040 physician signatures
  o  A petition to appeal the FDA warning

• Patient letters
  o  > 75,000 letters supporting epidural injections
  o  Letters opposing FDA policy
    ▪  > 3,800 to FDA
    ▪  > 12,000 to Congress

• Congressional support
  o  Physician Senators and DOC caucus
  o  Bicameral – Bipartisan support
Requested modification

• Withdraw the present Safety Warning
• Replace it with a Warning emphasizing:
  o Epidural steroids use is off-label and they can cause rare, but serious neurologic problems following cervical, thoracic, and lumbar transforaminal epidural injections
  o Are associated with an increased risk when performed without appropriate precautions, and
  o All procedures must be performed by well-trained providers in appropriate settings under fluoroscopy or computed tomography (CT).
Boxed Warning: Standards

“Strongest warning based on medical evidence”
• Serious adverse reactions
  o Fatal
  o Life threatening
• Preventable serious adverse reactions
  o Patient selection
  o Monitoring
  o Avoiding in specific clinical situation
• FDA approval with restrictions to assure safe use

FDA Guidelines for industry contains non-providing recommendations
Drug safety oversight board was concerned.
Interventional Pain Management

- American Society of Interventional Pain Physicians (ASIPP) founded in 1998
  - > 4000 members
  - Sole representation of IPM in USA
- MPW and other Organizations

If ASIPP membership were excluded, all 14 societies membership would include < 4,000 members

Super CAC: MPW process of LCDs.
Almost 100% non-compliance.
Effectiveness Boxed Warnings

• Antidepressants
  o ↓ use with ↑ suicides

• NSAIDs
  o ↑ Cox-1 inhibitor use with ↓ Cox-2 inhibitor use

• Opioids
  o ↑ regulations, use abuse and deaths
Issues of Epidural Steroid Warning

• Warning
  o Process and Methodology

• 17 recommendations / regulations

• Safe Use Initiative – no consensus for 20 regs/rec
  o MPW – consensus of 14 individual for 17regs/rec
  o Same organizations with different outcomes

• Misclassification
  o Extrapolation of evidence from cervical transforaminal 2% to all (98% - 100%)
  o Lack of evidence
  o Lack of consensus
  o Lack of transparency

Single policy – Based on single opinion – from a single person