Rash during Procedural Sedation for Trimalleolar Fracture

Saint John, Emergency Medicine Case Rounds – 10 October, 2017

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Learning points for discussion around...

- Response to possible drug reaction during procedural sedation
- Options for avoiding or mitigating histamine release reactions to opioids
Case

14 y/o M, healthy
Fall from bicycle ~ 1 hour prior to presentation to ED
No head injury, no LOC
C/o pain and swelling R. ankle
Unable to ambulate
Transport by EMS – pt splinted on route, extremity NVI, Entonox for analgesia
Case

In the ED....

- Entonox → Acetaminophen, Fentanyl
- closed R. ankle injury, remains NVI
- BP 145/72, P 90, S 96% RA, T 36.8
- off to xray he goes....
- Comminuted fractures, distal tibia + fibula
- Apex medial and posterior angulation
- Ankle and growth plate intact
Case

- Ortho consulted

- Ortho R3 arrives in ED to assist with reduction

- Full team: ED attending, ED resident, Emerg CC3, Ortho resident, RN, RN (training), RT, RT (student), LPN, X-Ray Tech
Case

Balanced Procedural Sedation with:

- Fentanyl
- Ketamine
- Propofol
Case

- ~ 20 minutes into procedure, macular rash noted over patients chest, progressing over abdomen
- no airway involvement, no hypotension or tachycardia
- decision made to treat with IV diphenhydramine and have epinephrine on hand
- meds for anaphylaxis not immediately available and nurse sent to retrieve

**smaller area of involvement than pictured**
Case

- Reduction completed within few minutes of rash presentation

- Rash resolved on own within ~15 minutes, diphenhydramine was never administered

- LPN commented that she had taken part in a previous procedural sedation for this patient ...“something was off then too”...

** smaller area of involvement than pictured
Post Reduction Imaging

- Not a perfect reduction
- Ortho opted for above the knee cast
- Decision was made not to reattempt reduction given likely medication reaction
Questions?

- Given the quick onset and resolution of macular rash during procedure, what would others have opted to do? Nothing, treat, reattempt, other?
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- What is the likely culprit for the rash?
Histamine Release with Opioids

- COMMON!!

- ‘Pseudoallergy’ – pts often get inappropriately labeled with allergy to entire opioid class, but this is a pharmacologic side effect

- Well known, with research dating back to early 1980s, but mechanism still not completely understood. Unlikely due to opioid receptor, activation of G proteins on mast cells leading to histamine release
<table>
<thead>
<tr>
<th>Pseudoallergy</th>
<th>True Allergy</th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ Flushing, itching, hives, sweating, and/or mild</td>
<td><strong>RARE!</strong> - change to non-opioid or an opioid from different chemical class</td>
</tr>
<tr>
<td>hypotension</td>
<td></td>
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<tr>
<td>▪ Itching, flushing or hives at injection site only</td>
<td></td>
</tr>
<tr>
<td></td>
<td>▪ <strong>Severe hypotension</strong></td>
</tr>
<tr>
<td></td>
<td>▪ <strong>Skin reaction</strong> other than flushing, itching, hives</td>
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<tr>
<td></td>
<td>▪ <strong>Breathing</strong>, speaking, swallowing difficulties</td>
</tr>
<tr>
<td></td>
<td>▪ <strong>Swelling of the face</strong>, lips, mouth, tongue, pharynx or larynx</td>
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Histamine Release with Opioids

- **Opioid Chemical Class**
  - **Phenylpiperidines:** meperidine, fentanyl, sufentanil, remifentanil
  - **Diphenylheptanes:** methadone, propoxyphene
  - **Morphine group:** morphine, codeine, hydromorphone, oxycodone, pentazocine

- **Opioid Intolerance**
  - Use of a more potent opioid less likely to release histamine.
  - Potency, from lower to higher:
    - meperidine < codeine < morphine < hydrocodone < oxycodone < hydromorphone < fentanyl
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<th>Management of Pseudoallergy</th>
<th>Management of True Allergy (Anaphylaxis)</th>
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<tr>
<td>- Optimize non-opioid analgesia</td>
<td>- Managed as any other anaphylaxis</td>
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<tr>
<td>- Reduce doses if possible</td>
<td>- Focus on airway and resuscitation</td>
</tr>
<tr>
<td>- Pretreat with H1 and H2 antihistamines</td>
<td>- Epinephrine!!</td>
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</tr>
<tr>
<td>- Bland moisturizers</td>
<td>- Corticosteroid</td>
</tr>
<tr>
<td></td>
<td>- Fluids</td>
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Ketamine

- Drug monographs list the following for Ketamine
  - Erythema (transient)
  - Morbilliform Rash (transient)
  - Rash at injection site
Ketamine

- Discussion of this phenomena in the literature dates back to the 1970s, but clinically, less well known than opioid histamine release.

- Prausnitz-Kustner (P-K) test (now replaced by skin prick test)
  - Not anaphylactic mechanism
  - Histamine release is pharmacologic effect of Ketamine directly stimulating mast cells

- Treatment is similar to what was previously discussed for opioids
Drug Monographs list the following for Propofol:

- Skin rash (children: 5%, adults 1%-3%)
- Pruritus (1%-3%)

Hypersensitivity reactions are more common in those with known reaction to eggs, soy, and peanut products.

Manufacturers contraindicate use in these circumstances, however retrospective studies suggest this is only clinically significant in cases of anaphylactic reaction to these substances.
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- What is the likely culprit for the rash?

- What are the consequences immediate or long-term for the patient?
My own learning points…

- Drug rashes are common and every drug monograph will include them, but temporality matters!
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• Choosing to do nothing is still a decision, and sometimes it’s the right one.
My own learning points...

• Drug rashes are common and every drug monograph will include them, but temporality matters!

• Choosing to do nothing is still a decision, and sometimes it’s the right course of action.

• Working as a multidisciplinary team is helpful; everyone can focus on what they do best and some responsibility can be offloaded to the consulting service.
References


• Mathieu A, Goudsouzian M, Snider T. Reaction to ketamine: anaphylactoid or anaphylactic? *BJA*. 1975;47(5): http://doi.org/10.1093/bja/47.5.624


Post-Op Imaging