Disclosure

- The program chair and presenters for this continuing education activity have reported no relevant financial relationships.
<table>
<thead>
<tr>
<th>Nadia Awad</th>
<th>Megan Musselman</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zlatan Coralic</td>
<td>Andrew North</td>
</tr>
<tr>
<td>Katelyn Dervay</td>
<td>John Patka</td>
</tr>
<tr>
<td>Meghan Groth</td>
<td>Cassey Peters</td>
</tr>
<tr>
<td>Kathleen McDermott</td>
<td>Denise Pratt</td>
</tr>
<tr>
<td>Aimee Mishler</td>
<td>Brittany Traylor</td>
</tr>
</tbody>
</table>

Tweet Your Questions

@PharmERToxGuy
Part 1
Antidote Stewardship: Possible Role for Carbapenems in Valproic Acid Toxicity

Colgan “Cole” Sloan, Pharm.D., BCPS
Clinical Pharmacist – Emergency Medicine
University of Utah Health Care
Twitter @DrugInfoGeek
Learning Objective

- Assess the risks and benefits of using a carbapenem to treat valproic acid toxicity
Introduction

- One of the coolest drug interactions... ever
  - Case report if it does not occur

- Several proposed mechanisms for this drug-drug interaction (DDI)
POTENTIAL Toxicologic Use

- Could this interaction treat valproic acid (VPA) toxicity?

- Effects of the DDI may persist

- Remember your ABCs

- One report, thus far, of intentionally using this DDI for VPA overdose
Considerations

- Reason for VPA

- Other therapies for VPA toxicity
  - Supportive care
  - Activated charcoal
  - Levocarnitine
  - Hemodialysis
  - Tincture of time

- Won’t address all sequelae of VPA toxicity
Which Carbapenem

- All available carbapenems associated with this DDI
  - Availability
  - Pharmacokinetics
  - Duration

- Imipenem-Cilastatin, greater risk of seizures?
  - Imipenem (7/1124) vs meropenem (4/1116)
  - Odds Ratio 1.48 (0.54, 4.04)

Key Takeaways

▪ Key Takeaway #1
  • Consider patient specific factors and adverse event potential before using a carbapenem to treat VPA toxicity

▪ Key Takeaway #2
  • Use of a carbapenem is unlikely to treat all complications of serious VPA toxicity – do not eschew the basic management of toxicology patients

▪ Key Takeaway #3
  • If you undertake this approach, write the case up; there are many unknowns with using this DDI in toxicology
References

- Zosel, et al. Novel use of ertapenem to intentionally decrease serum valproate concentration after an intentional overdose of valproate resulting in toxicity. NACCT 2015 Poster #106. Link

Presenter’s Email: cole.sloan@gmail.com  Twitter: @DrugInfoGeek
Laboratory Monitoring to Determine the Presence of DOACs

Emily Kilber, PharmD
PGY2 EM Pharmacy Resident
The University of Arizona
Objective

- Identify specific laboratory tests to aid in detecting the presence of direct oral anticoagulants (DOAC)
Imagine...

- 55 year old male
- Unresponsive
- Unknown PMH
- CT scan: SDH
Oral Anticoagulants

- **Vitamin K Antagonist**
  - Warfarin

- **DOACs**
  - Dabigatran
  - Rivaroxaban
  - Apixaban
  - Edoxaban

Monitor with INR

Unclear monitoring
<table>
<thead>
<tr>
<th>DOAC</th>
<th>aPTT</th>
<th>PT</th>
<th>TT</th>
<th>Anti-Xa</th>
<th>Other Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dabigatran</td>
<td>++</td>
<td>+</td>
<td>+++</td>
<td>--</td>
<td>dTT, DTI, ECT, ECA, ACT</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>+</td>
<td>++</td>
<td>--</td>
<td>++</td>
<td>None</td>
</tr>
<tr>
<td>Apixaban</td>
<td>-/+</td>
<td>-/+</td>
<td>--</td>
<td>++</td>
<td>None</td>
</tr>
</tbody>
</table>

ACT, activated clotting time; aPTT, activated partial thromboplastin assay; DTI, direct thrombin inhibitor (assay); dTT, dilute thrombin time; ECA, ecarin chromogenic assay; ECT, ecarin clotting time; PT, prothrombin time; TT, thrombin time

TT, PT, aPTT

- **↑ aPTT and TT**
  - Dabigatran

- **↑ PT**
  - TT normal
    - Rivaroxaban
    - Apixaban or Edoxaban

- **All normal**
  - Anti-Xa activity
References

Use of Ketamine in Resistant Alcohol Withdrawal

Linda Barstow, PharmD
PGY2 Emergency Medicine Pharmacy Resident
University of Maryland Medical Center
Baltimore, MD
Learning Objective

- To identify the role of ketamine for treatment of alcohol withdrawal syndrome (AWS)

Photo: http://www.acesurgical.com/ketamine-50mg-ml-10ml-injection.html
Pathophysiology & Symptoms

- Hypertension, tachycardia, tachypnea, hyperpyrexia
- Anxiety, tremor, tongue fasciculations, diaphoresis
- Delirium, seizures, death
- Severity difficult to predict

Ind Psychiatry J. 2013;22(2):100-108
Ann of Pharm. 2015;49(1):14-19
Current Treatment

Ind Psychiatry J. 2013;22(2):100-108
First Line Treatment

- Benzodiazepines
  - Diazepam, lorazepam, chlordiazepoxide

Arch Intern Med. 2004;164: 1405-1412
Ann of Pharm. 2015;49(1):14-19
Photo: neuroscience/behavioral-and-psychiatric-disorders-integrative-systems
Resistant Alcohol Withdrawal (RAW)

- Definition by treatment requirement
  - 1 hour: > 50mg diazepam or > 10mg lorazepam
  - 4 hours: > 200mg diazepam or > 40mg lorazepam
- Pathophysiology poorly understood
  - Endogenous GABA neurotransmitter depletion
  - Profound down-regulation and/or altered structure of GABA receptors

Crit Care Med. 2007;35(3)724-30
Pharmacother. 2016; epub ahead of print
Barbiturates (phenobarbital)
- Alternative agent of choice
- Increases duration GABA channel is open

Dexmedetomidine
- Selective $\alpha_2$ agonist
- Does not treat underlying mechanism

Propofol
- GABA agonist activity at alternative receptor site
  - GABA independent
- NMDA receptor antagonism
Wong et al.

- Purpose: Evaluate use of adjunctive ketamine for management of severe AWS
- Study Design: Retrospective cohort study of adult patients administered ketamine for AWS
  - LD (when used): 0.3 mg/kg
  - Mean initial infusion rate: 0.21 mg/kg/hr
  - Mean total infusion rate: 0.20 mg/kg/hr

Ann Pharmacother. 2015; 49(1)14-19
Wong et al.

- **Results**
  - Twenty three patients qualified for inclusion
  - Median change in benzodiazepine requirements
    - 12H after infusion: -40.0 mg, p=0.110
    - 24H after infusion: -13.3 mg, p=0.330
  - Median (IQR) change in sedation scores
    - WAS (n=8): +1.0 (-4.5, +2.0)
    - SAS (n=5): +1.0 (0, +2.0)
  - Ketamine-related adverse reactions
    - Over-sedation requiring dose reduction (n=1)
Wong et al.

- Limitations
  - Additional agents used
  - Sample size (n=23)

- Application
  - Who? Under what circumstances?
  - How, and for how long?
  - What next?
References

- Gold et al. A strategy for escalating doses of benzodiazepines and phenobarbital administration reduces the need for mechanical ventilation in delirium tremens. Critical Care Medicine. 2007;35(3)724-30
Key Takeaways

- **Key Takeaway #1**
  - Ketamine should only be used in conjunction with standard benzodiazepine therapy after all other alternatives are exhausted

- **Key Takeaway #2**
  - A reasonable approach to dosing would replicate that of Wong et al
    - LD (when used): 0.3 mg/kg
    - Mean initial infusion rate: 0.21 mg/kg/hr
Peripheral Vasopressors: A Quick Fix Worth The Risk?

Matt Bilhimer Pharm.D.
Emergency Medicine Clinical Pharmacist
Salina Regional Health Center
Salina, KS
Objectives

- Identify concerns regarding vasopressor administration in the emergency department (ED)
- Understand current evidence describing safety of vasopressors administered via peripheral and central lines
We’ve All Been There...

GET ME NOREPI!!!
Issues In The Emergency Department (ED)

- Emergent Need

- Route of Administration
  - Central line: preferred but not always available
  - Peripheral line: easily accessible but greater risk → Extravasation

Prioritize – Perfusion vs. Extremity
Techniques to Reduce Extravasation Risk

- Avoid infusion in small diameter vessels
- Low vs. high concentration products
- Administer via Y-site with IV fluids running
### Time to Local Tissue Injury with Peripheral Line (n = 138*)

<table>
<thead>
<tr>
<th>Duration of Infusion Until Complication Noted</th>
<th>Number of Local Tissue Injury Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1 hr</td>
<td>1</td>
</tr>
<tr>
<td>1 - 2 hrs</td>
<td>3</td>
</tr>
<tr>
<td>2 - 3 hrs</td>
<td>3</td>
</tr>
<tr>
<td>3 - 4 hrs</td>
<td>0</td>
</tr>
<tr>
<td>4 - 5 hrs</td>
<td>1</td>
</tr>
<tr>
<td>5 - 6 hrs</td>
<td>1</td>
</tr>
<tr>
<td>6 - 12 hrs</td>
<td>9</td>
</tr>
<tr>
<td>12 - 24 hrs</td>
<td>18</td>
</tr>
<tr>
<td>≥ 24 hrs</td>
<td>102</td>
</tr>
</tbody>
</table>

*66 patients with no time to event information

Loubani OM, Green RS. J Crit Care 2015. 653.e-653e.17
## Long Term Sequelae: Peripheral Vasopressors

<table>
<thead>
<tr>
<th>Long-term Adverse Effect</th>
<th>Local Tissue Injury (n = 204*)</th>
<th>Extravasation (n = 114*)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None, no. (%)</td>
<td>77 (37.7)</td>
<td>90 (78.9)</td>
</tr>
<tr>
<td>Minor Disability, no. (%)</td>
<td>36 (17.6)</td>
<td>1 (0.9)</td>
</tr>
<tr>
<td>Major Disability, no. (%)</td>
<td>9 (4.4)</td>
<td>3 (2.6)</td>
</tr>
<tr>
<td>Mortality – related to pressor event, no. (%)</td>
<td>4 (2)</td>
<td>1 (0.9)</td>
</tr>
</tbody>
</table>

*98 patients total with mortality unrelated to pressor event or long-term sequelae not reported

Loubani OM, Green RS. J Crit Care 2015. 653.e-653e.17
Conclusion

Vasopressors may be safely administered via a peripheral line when infused for a short period (i.e., < 6 hours) through proximal sites
You Want To Do What?! 
ECMO in the ED 

Giles W. Slocum, Pharm.D. 
Clinical Pharmacy Specialist, Emergency Medicine 
Rush University Medical Center
Learning Objectives

I. Describe the role of a clinical pharmacist when starting extracorporeal membrane oxygenation (ECMO) in the emergency department

II. Recognize the pharmacokinetic changes on commonly used medications when starting ECMO in the ED
There has never been a medication that has shown any long term survival benefit in cardiac arrest
Okay… so what works?

- Quality chest compressions
- Electrical defibrillation

... 

- Extracorporeal membrane oxygenation
- Extracorporeal cardiopulmonary resuscitation (ECPR)
- Extracorporeal life support (ECLS)

Venoartial-ECMO (VA)  
Venovenous-ECMO (VV)  

- Femoral Artery  
- Internal Jugular Vein  
- Returning Oxygenated Blood  
- De-oxygenated Blood  

Pharmacy role in ECMO

Anticoagulation

Pharmacokinetics

- Absorption
  - Drug sequestration
- Distribution
  - Increased volume of distribution
- Metabolism
  - Reduced bloodflow
- Elimination
  - Decreased clearance

Final thoughts

We may see an increase in ECLS as medications are removed from our ACLS algorithms

Ensure appropriate and adequate anticoagulation

Monitor patient and adjust medications as necessary to account for pharmacokinetic changes
Tweet Your Questions

@PharmERToxGuy
True or False Statement

All broad-spectrum antibiotics, e.g. piperacillin-tazobactam, tigecycline, daptomycin - have a role in treating valproic acid toxicity.

A  TRUE
B  FALSE
True or False Statement

All broad-spectrum antibiotics, e.g. piperacillin-tazobactam, tigecycline, daptomycin - have a role in treating valproic acid toxicity.

A. TRUE
B. FALSE
(True or False) Prothrombin time prolongation is the most specific indicator of the presence of dabigatran

A  TRUE
B  FALSE
(True or False) Prothrombin time prolongation is the most specific indicator of the presence of dabigatran

A TRUE
B FALSE
Which of the following pathophysiologic mechanisms of alcohol dependence does ketamine target?

A. Down-regulation of inhibitory GABA receptors
B. Up-regulation of excitatory NMDA receptors
Which of the following pathophysiologic mechanisms of alcohol dependence does ketamine target?

A. Down-regulation of inhibitory GABA receptors

B. Up-regulation of excitatory NMDA receptors
Which of the following may *increase* your patient’s risk of experiencing local tissue injury or extravasation when receiving vasopressors through a peripheral IV?

- **A** IV sites proximal to the antecubital vein or popliteal fossa
- **B** Infusion duration greater than 24 hours
- **C** Administration of lower concentration products
- **D** All of the above
Which of the following may increase your patient’s risk of experiencing local tissue injury or extravasation when receiving vasopressors through a peripheral IV?

A. IV sites proximal to the antecubital vein or popliteal fossa
B. Infusion duration greater than 24 hours
C. Administration of lower concentration products
D. All of the above
ECMO changes the pharmacokinetic properties of medications in these ways, EXCEPT:

A. Increased absorption
B. Decreased elimination
C. Increased volume of distribution
D. Decreased metabolism
ECMO changes the pharmacokinetic properties of medications in these ways, EXCEPT:

- A. Increased absorption
- B. Decreased elimination
- C. Increased volume of distribution
- D. Decreased metabolism
Part 2
Burnout Syndrome

Patrick Bridgeman PharmD, BCPS
Clinical Assistant Professor
Program Director PGY-2 Emergency Medicine Pharmacy Residency
Ernest Mario School of Pharmacy
Learning Objective

- Identify strategies to help reduce the possibility of burn out
What is Burnout Syndrome (BOS)

- Maslach Burnout Inventory (MBI)
  - Diagnosed when exceed cut off
- Depersonalization
- Emotional exhaustion
- Decreased sense of accomplishment

Risk Factors for Developing BOS

- Four categories
  - Personal characteristics
  - Organizational factors
  - Quality of working relationships
  - Exposure to end of life issues

Consequences of BOS

- Decreased performance
- Poor patient outcomes
- Poor patient satisfaction
- Poor personal health (obesity, substance abuse)


Preventing Burnout

- Be responsible for yourself
- Adequate Rest
- Exercise
- Meditation
- Hobbies
- Find a Buddy
Concluding Points

- BOS is a common occurrence in the health professions
- It is your responsibility
- Be aware of causes of burnout
Red Out, Red In
Cyanide toxicity in the ED

Hina Patel, PharmD, BCPS
Senior Clinical Specialist, Emergency Medicine
PGY1 Pharmacy Residency Program Director
NorthShore University HealthSystem
Objective

- Review the use of hydroxocobalamin for acute cyanide toxicity and its impact on laboratory analyses of fluid samples
The presentation

28 yo otherwise healthy male firefighter presents to the ED after prolonged smoke inhalation during a multi-unit residential fire.

Initial symptoms:

- Cough/SOB
- Headache
- Pulse ox 88%
- Soot in upper airway

- Tachycardia
- Nausea
The presentation

- Carboxyhemoglobin levels:
  - Time zero (at site): 12%
  - 15 minutes later (at hospital): 3%
  - 30 minutes later: < 1.5%

- Chest radiograph reveals mild pulmonary edema
- Normal skin appearance
- Initial ABG reveals respiratory acidosis
- Supplemental oxygen 100% administered
- NS started at 200 ml/hr
Initial laboratory results

Notable:
Anion gap: 28 ↑
Lactic acid: 8.5 mmol/L ↑
Methemoglobin: 2.8% ↔
BMP, CBC WNL

Nurse noted that venous blood draw was unusually bright red.
Suspected diagnoses and treatment

- Potential for acute cyanide toxicity
- Hydroxocobalamin 5 grams IV STAT ordered
- RN mixes and begins 200 ml infusion over 15 minutes
- MD requests additional blood to be drawn to check liver and coagulation panels, second ABG, UA
Next lab results

Lab results post for additional tests

- Liver panel: ALT = 2 (↓); total bilirubin 4.1 (↑)
- PT/INR: POC test resulted in ‘error’; blood pending
- Repeat ABG: pH 7.52 (↑) (compared to initial pH 7.38)
- UA: WNL except for “pink tinged”

Question: Is the patient sicker than we thought?
Hydroxocobalamin

- Chelates cyanide
  - Exchanges 1:1 CN- with hydroxo ligand bound at cobalt ion
  - Cyanocobalamin excreted in urine

- Side effects
  - Transient hypertension, pink discoloration of skin, mucous membranes, urine, feces

- Light absorption characteristics affect laboratory assays that use colorimetric or reduced NAD or NADP reactions
# Laboratory interferences

<table>
<thead>
<tr>
<th>Laboratory Parameter</th>
<th>No Interference Observed</th>
<th>Artificially Increased *</th>
<th>Artificially Decreased *</th>
<th>Unpredictable</th>
<th>Duration of Interference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Chemistry</td>
<td>Calcium</td>
<td>Creatinine</td>
<td>ALT</td>
<td>Phosphate</td>
<td>24 hours with the</td>
</tr>
<tr>
<td></td>
<td>Sodium</td>
<td>Bilirubin</td>
<td>Amylase</td>
<td>Uric Acid</td>
<td>exception of bilirubin</td>
</tr>
<tr>
<td></td>
<td>Potassium</td>
<td>Triglycerides</td>
<td></td>
<td>AST</td>
<td>(up to 4 days)</td>
</tr>
<tr>
<td></td>
<td>Chloride</td>
<td>Cholesterol</td>
<td></td>
<td>CK</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Urea</td>
<td>Total protein</td>
<td></td>
<td>CKMB</td>
<td></td>
</tr>
<tr>
<td></td>
<td>GGT</td>
<td>Glucose</td>
<td></td>
<td>LDH</td>
<td></td>
</tr>
<tr>
<td></td>
<td>BUN</td>
<td>Albumin</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Alkaline phosphatase</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Magnesium</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

* ≥10% interference observed on at least 1 analyzer

# Laboratory interferences

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<th>Artificially Decreased*</th>
<th>Unpredictable</th>
<th>Duration of Interference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hematology</strong></td>
<td>Erythrocytes</td>
<td>Hemoglobin</td>
<td></td>
<td></td>
<td>12 – 16 hours</td>
</tr>
<tr>
<td></td>
<td>Hematocrit</td>
<td>MCH</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>MCV</td>
<td>MCHC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Leukocytes</td>
<td>Basophils</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Lymphocytes</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Monocytes</td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>Eosinophils</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Neutrophils</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Platelets</td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>Coagulation</strong></td>
<td></td>
<td></td>
<td>aPTT</td>
<td></td>
<td>24 – 48 hours</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>PT (Quick or INR)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* ≥10% interference observed on at least 1 analyzer

## Laboratory interferences

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<thead>
<tr>
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<th>Artificially Decreased*</th>
<th>Unpredictable</th>
<th>Duration of Interference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinalysis</td>
<td></td>
<td>pH (with all doses)</td>
<td>pH (with equivalent doses of &lt;5 g)</td>
<td></td>
<td>48 hours up to 8 days; color changes may persist up to 28 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Glucose</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Protein</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>erythrocytes</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Leukocytes</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td>Ketones</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Bilirubin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Urobilinogen</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nitrite</td>
<td></td>
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<tr>
<td>Cooximetry</td>
<td></td>
<td>Oxyhemoglobin</td>
<td>Total hemoglobin</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Carboxyhemoglobin</td>
<td>Methemoglobin</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* ≥10% interference observed on at least 1 analyzer

Back to the patient

- Intubated for airway protection
- Some improvement in oxygenation post hydroxocobalamin
- Transferred to tertiary burn center for further management
- Received call from receiving center to inquire exact time of antidote administration
- Full recovery and discharge 2 days later
Key Takeaways

- Suspecting cyanide toxicity? Collect all bodily fluid samples before administering hydroxocobalamin
- Re-evaluate unexpected results relative to administration of antidote
- Don’t forget to tell the next provider
Lopesick

Colleen Martin, PharmD, BCPS
Clinical Pharmacist, Emergency Medicine
Nyack Hospital, Nyack, NY
Learning Objective

- Describe the presentation and management of loperamide toxicity
MF is a 30 yo male, presents to ED after syncopal episode at work

ECG shows sinus rhythm, with prolonged QT and QRS

Patient reports “I sometimes take loperamide, nothing else, really.”
Should I be worried about loperamide?
Mechanism of Loperamide

Legend

- μ receptor
- loperamide

intestinal wall

acetylcholine

prostaglandins
Abuse Potential

P-glycoprotein
“...200mg of lope (100 pills) will make me almost 100[%] again” “If you take a sh**load of lope like 10 - 20 pills at once in withdrawal, you’ll get relief...”

“I just went out and bought a ton of loperamide and Tagamet* because I’ve been reading how much it helps”

“I started taking 100 mgs of loperamide...taken orally with 800mg of Tagamet*”
FDA Drug Safety Communication: FDA warns about serious heart problems with high doses of the antidiarrheal medicine loperamide (Imodium), including from abuse and misuse
Clinical Presentation

- Syncope
- QRS and QT prolongation
  - Ventricular arrhythmias
  - Cardiac arrest
- Shortness of breath
Evaluation

Comprehensive metabolic panel

Continuous cardiac monitor

Loperamide level
Key Takeaways

- Loperamide has the potential for abuse
- Loperamide abuse can lead to cardiac toxicity
Give Me Some Suga!

Jenny Koehl, Pharm.D.
PGY2 Emergency Medicine Resident
UW Health
Madison, WI
Learning Objective:

• Describe the utility of sugammadex for reversing rocuronium in the emergency department
Urgent Reversal of Rocuronium

Neostigmine + glycopyrrolate

Sugammadex

2007 FDA Rejected

2012 FDA Rejected

2015 FDA Approved
Potential Uses of Sugammadex in the Emergency Department

• Unexpected difficult airway / can’t intubate, can’t ventilate situations
  ▪ Reversal for physical exams
  ▪ Reversal in status epilepticus
  ▪ Allergic reaction to rocuronium or vecuronium
Administration Feasibility

2.7 minute time difference

100 kg patient = 1,600 mg

200mg/2 mL vial: 8 vials
500mg/5 mL vial: 4 vials

Lee C. Anesthesiology. 2009;110(5):1020-1025
Side Effects

Side effect risk:
• Nausea 10.6%
• Pruritus 7.3%
• Urticaria 6%
• Anaphylaxis 0.024-0.33%
• Bradycardia – has led to cardiac arrest
• Doesn’t the patient still need an airway?

<table>
<thead>
<tr>
<th>NMBA Re-administration Following 16mg/kg Sugammadex Reversal</th>
<th>Minimum waiting time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rocuronium (any dose)</td>
<td>24 hours</td>
</tr>
<tr>
<td>Vecuronium (any dose)</td>
<td>24 hours</td>
</tr>
</tbody>
</table>
Key Takeaways

- 16mg/kg sugammadex can rapidly reverse high-dose rocuronium
- More drug cost, more medication exposure, more side effects
- Do not reverse paralysis in patients who require paralysis
- Utility in the emergency department is limited
Jenny Koehl, Pharm.D.
PGY2 Emergency Medicine Resident
UW Health
Madison, WI

jkoehl@uwhealth.org
IV Olanzapine: An atypical option for acute agitation?

Greta Astrup, Pharm.D.
PGY2 Emergency Medicine Pharmacy Resident
University of New Mexico Hospital
December 7th, 2016
Learning Objective

- Understand the evidence and recognize special considerations for the use of IV olanzapine as an alternative agent for the treatment of acute agitation in the Emergency Department.
Treatment

Causes of Agitation:
- Alcohol ingestion/withdrawal
- CNS infection
- Dementia
- Drug use/overdose
- Electrolyte abnormalities
- Hypoglycemia
- Hypoxia
- ICH/tumor
- Pain
- Seizure

IV Options:
- haloperidol
- ketamine
- lorazepam/midazolam
- IV olanzapine

Imminent threat to self or others?
- Yes
- No

IV Access?
- Yes
- No

Causes?
- Yes
- No

Agitated patient
## Evidence

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Design</th>
<th>Treatment</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chan EW et al. (2011)</td>
<td>4</td>
<td>Case reports</td>
<td>IV olanzapine 5-10 mg</td>
<td>Limited Sedation documented w/in ~30 min</td>
</tr>
<tr>
<td>Chan EW et al. (2013)</td>
<td>336</td>
<td>Randomized, double-blind, placebo-controlled, double-dummy</td>
<td>IV droperidol 5 mg, IV olanzapine 5 mg, or Placebo + IV midazolam 2.5-5 mg</td>
<td>IV droperidol/olanzapine with midazolam is effective and decreases time to sedation</td>
</tr>
<tr>
<td>Martel ML et al. (2016)</td>
<td>713</td>
<td>Retrospective review</td>
<td>IV olanzapine 1.25-10 mg</td>
<td>Safe in various ED indications</td>
</tr>
</tbody>
</table>

Considerations

- QTc prolongation
- Hypoventilation/ hypoxia
- Extrapyramidal symptoms (EPS)
- Dilution with SWFI required
Comparison

<table>
<thead>
<tr>
<th></th>
<th>Haloperidol</th>
<th>Olanzapine</th>
<th>Ziprasidone</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dosing</strong></td>
<td>IV: 0.5-10 mg</td>
<td>IV: 2.5-5 mg</td>
<td>IM: 10-20 mg</td>
</tr>
<tr>
<td></td>
<td>IM: 2.5-10 mg (Max: 20-30 mg/day)</td>
<td>IM: 5-10 mg (Max: 30 mg/day)</td>
<td>(Max: 40 mg/day)</td>
</tr>
<tr>
<td><strong>Onset</strong></td>
<td>IV: 5-10 min</td>
<td>IV: unknown</td>
<td>IM: 15-20 min</td>
</tr>
<tr>
<td></td>
<td>IM: 30-60 min</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Adverse effects</strong></td>
<td>- Sedation</td>
<td>- Sedation</td>
<td>- Nausea</td>
</tr>
<tr>
<td></td>
<td>- Hypotension</td>
<td>- HA</td>
<td>- HA</td>
</tr>
<tr>
<td></td>
<td>- Dysrhythmias and QTc</td>
<td>- Hypotension</td>
<td>- Dose related</td>
</tr>
<tr>
<td></td>
<td>prolongation</td>
<td>- QTc prolongation</td>
<td>dysrhythmias and QTc</td>
</tr>
<tr>
<td></td>
<td>- High EPS potential</td>
<td>- EPS</td>
<td>prolongation</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- EPS</td>
</tr>
</tbody>
</table>
Key Takeaways

- Key Takeaway # 1
  - IV olanzapine may be a potential option for acute agitation in the ED
    - Especially in patients at higher risk for QTc prolongation

- Key Takeaway # 2
  - Dosing: 2.5-5 mg IV
  - Requires reconstitution with SWFI
Tweet Your Questions

@PharmERToxGuy

Q & A Part 2
Which of the following are appropriate strategies to help prevent or treat burnout?

A. Exercise
B. Ensuring adequate sleep
C. Eating healthy
D. All of the above
Which of the following are appropriate strategies to help prevent or treat burnout?

A Exercise
B Ensuring adequate sleep
C Eating healthy
D All of the above
Assessment Question (True or False)

Presence of hydroxocobalamin can affect laboratory analyses of some clinical chemistries, hematology panels, and urinalyses?

A  TRUE
B  FALSE
Assessment Question (True or False)

Presence of hydroxocobalamin can affect laboratory analyses of some clinical chemistries, hematology panels, and urinalyses?

A  TRUE
B  FALSE
MF is a 30 yo male, presents to ED after syncopal episode at work

ECG shows sinus rhythm, with prolonged QT and QRS

Patient reports “I sometimes take loperamide, nothing else, really.”
Based on the patient’s history and presentation, what would be your next step(s)?

- Review comprehensive metabolic panel
- Monitor patient with continuous cardiac monitor
- Interview patient regarding loperamide use
- All of the above
Based on the patient’s history and presentation, what would be your next step(s)?

- Review comprehensive metabolic panel
- Monitor patient with continuous cardiac monitor
- Interview patient regarding loperamide use
- All of the above
What is the Most Common Side Effect of Sugammadex?

A. Bradycardia
B. Urticaria
C. Nausea/vomiting
D. Anaphylaxis
What is the Most Common Side Effect of Sugammadex?

A. Bradycardia
B. Urticaria
C. Nausea/vomiting
D. Anaphylaxis
Can Rocuronium be Re-administered Immediately After Sugammadex is Given?

A  YES
B  NO
Can Rocuronium be Re-administered Immediately After Sugammadex is Given?

A  YES
B  NO
Assessment Question

Which of the following are TRUE?

- A. Haloperidol is only FDA approved for IM administration
- B. IV olanzapine has been used safely and effectively in multiple case reports
- C. Olanzapine has less associated QTc effects compared to haloperidol
- D. All of the above
Assessment Question

Which of the following are TRUE?

A. Haloperidol is only FDA approved for IM administration
B. IV olanzapine has been used safely and effectively in multiple case reports
C. Olanzapine has less associated QTc effects compared to haloperidol
D. All of the above
Juliana Zschoche
Emily Pavich
Ashley Niemczyk  @ashleyrniemczyk
Eric Kanouse
Daniel Paley

Part 3
Should we say goodbye to succinylcholine use in traumatic brain injury patients?

Juliana Zschoche, PharmD
Clinical Pharmacy Specialist – Emergency Medicine
The Johns Hopkins Hospital
Baltimore, Maryland
Learning Objective

- Discuss the evidence and clinical implications of the use of succinylcholine as a paralytic in patients with traumatic brain injuries.
Traumatic Brain Injury

- Traumatic brain injury (TBI)
  - Craniocerebral trauma associated with neurological or neuropsychological abnormalities, skull fracture, intracranial lesions or death

- Injuries
  - Concussion
  - Skull Fracture
  - Contusion
  - Subdural Hematoma
  - Subarachnoid Hemorrhage

Intracranial Pressure (ICP)

Causes of elevated ICP in trauma
- Increase in volume of any or all of the intracranial components
- Excessive cerebral blood flow
- Hypercapnia or hypoxia causing vasodilation and increase cerebral blood flow
- Herniation, brain swelling, or subarachnoid hemorrhage

\[
\text{CPP} = \text{MAP} - \text{ICP}
\]
Treatment of TBI

- Initial Stabilization
  - Airway Management
    - Adequate Ventilation
      - Rapid Sequence Intubation
  - Circulatory Support
- Elevated ICP Management
- Hemodynamic Support
- Analgesia and Sedation
- Seizure Prophylaxis
Succinylcholine

- Depolarizing neuromuscular blocking agent
- Quick onset, short duration of action
- Adverse Drug Reactions
  - Hyperkalemia
  - Muscle fasciculation
  - Bradycardia/hypotension
  - Malignant hyperthermia
  - Increase in ICP
- Avoid use in burn patients, patients with crush injuries, and patients with renal failure or on dialysis
Succinylcholine increase ICP?

- May be associated with a transient increase in ICP
  - FDA Labeling

- Mechanism: Unknown
  - Hypothesis: Mediated via an increase in afferent spinal neural traffic origination from muscle spindle fibers, followed by an increased in cerebral blood flow

Previous Studies

  - Succinylcholine caused a significant elevation in ICP during induction in 8 adult patients who were to undergo craniotomy

- Anesth Analg 1994; 78:469-73
  - Succinylcholine use caused no change in cerebral perfusion pressure, mean arterial pressure, or intracranial pressure in 10 mechanically ventilated patients being treated for elevated ICP
**Succinylcholine vs Rocuronium**

Succinylcholine Is Associated with Increased Mortality When Used for Rapid Sequence Intubation of Severely Brain Injured Patients in the Emergency Department

<table>
<thead>
<tr>
<th>Population</th>
<th>233 patients with TBI who underwent RSI with succinylcholine (n = 149 pts) or rocuronium (n = 84 pts) Subjects were stratified based upon on severity of injury using head abbreviated injury scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Outcome</td>
<td>In-hospital mortality</td>
</tr>
<tr>
<td>Intervention</td>
<td>Retrospective cohort study: succinylcholine versus rocuronium as NMBA in patients from October 2010 to October 2014</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Results</th>
<th><strong>Intervention</strong></th>
<th><strong>Mortality (%)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Succinylcholine</td>
<td>23</td>
</tr>
<tr>
<td></td>
<td>Low-severity TBI (14/103)</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>High-severity TBI (20/46)</td>
<td>44</td>
</tr>
<tr>
<td></td>
<td>Rocuronium</td>
<td>23</td>
</tr>
<tr>
<td></td>
<td>Low-severity TBI (12/54)</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>High-severity TBI (7/30)</td>
<td>23</td>
</tr>
</tbody>
</table>

Succinylcholine vs Rocuronium

- Significant statistical interaction was noted between head AIS and NMBA choice
  - OR 4.10, 95% CI 1.18–14.12
- Effect of succinylcholine on mortality was significant only in patients with severe or critical TBI
- Head abbreviated injury score is a subjective assessment that cannot be performed in real time prior to intubation
- Cannot correlate GCS to head abbreviated injury score
- Other limitations

Key Takeaways

- **Key Takeaway #1**
  - Succinylcholine may cause a mild increase in intracranial pressure, but the clinical significance is unknown.

- **Key Takeaway #1**
  - Succinylcholine use for RSI in patients with severe traumatic brain injury may be associated with increased mortality.

- **Key Takeaway #3**
  - It is difficult to discriminate reliably which patients are likely to benefit from avoidance of succinylcholine at the time of intubation in the emergency department.
An NIHSS of 2 for confusion: Did the ischemic stroke guidelines change?

Emily Pavich, PharmD
Emergency Medicine Clinical Pharmacist
Indiana University Health Bloomington Hospital
Learning objective

- Compare the American Heart Association/American Stroke Association (AHA/ASA) scientific statement of rationale for inclusion and exclusion criteria for intravenous alteplase in acute ischemic stroke (AIS) with key changes made in the alteplase package insert (PI)
BS is a 75 yo M presenting to the ED with acute onset of dizziness, inability to walk, and nausea. Onset was 1.5 hours ago.

NIHSS = 2 for limb ataxia
Blood glucose 92 mg/dL
Blood pressure 150/68 mm Hg
No anticoagulant use at home
CT scan shows no acute intracranial hemorrhage (ICH)

PMH: Patient was diagnosed with posterior circulation stroke at outside facility 3 weeks ago, where he received alteplase
That’s why I keep the PI in my pocket!
#micdropboom #winning #alteplaseconquersall #clotbusted

10:30 PM – 26 Jan 2016

Disclaimer: This is not or was not ever an actual Tweet
Timeline of alteplase in stroke updates

- **2013**
  - AHA/ASA guidelines for patients with AIS

- **Feb 2015**
  - FDA Physician Labeling Rule (PLR) changes made to alteplase PI

- **Dec 2015**
  - AHA/ASA rationale for IV alteplase inclusion and exclusion criteria

Genentech Medical Communications, e-mail; September 2015.
## Alteplase PI contraindication section changes

### Absolute contraindications removed

- Previous stroke in the preceding 3 months
- History of ICH
- Arterial puncture at non-compressible site in previous 7 days
- CT demonstrates multilobar stroke
- Blood Glucose < 50 mg/dL

### Absolute contraindications changed

- Symptoms suggestive of SAH
- BP $\geq 185$ / $\geq 110$ mm Hg
- Anticoagulant use and INR $> 1.7$ or PT $> 15$ seconds
- Heparin or LMWH use and aPTT $> 40$ seconds
- Platelet count $> 100,000$/mm$^3$
- Current use of DTIs or FXals w/ elevated sensitive tests

- All relative contraindications were removed from the PI contraindications

Hashtag worthy?

- Physician Labeling Rule (PLR):
  “Only known hazards, and not theoretical possibilities, can be the basis for a contraindication”

- 2015 AHA/ASA Scientific Rationale Statement:

  “...The PI changes were made by the FDA in the context of no substantial new information...”

Genentech Medical Communications, e-mail; September 2015.
## AHA/ASA scientific statement for removed and amended contraindications

<table>
<thead>
<tr>
<th>Absolute contraindication removed or changed in the PI</th>
<th>AHA/ASA 2015 statement &amp; evidence level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multilobar infarction (hypodensity &gt; 1/3 cerebral hemisphere)</td>
<td>No threshold evidence, these patients have poor prognosis (A)</td>
</tr>
<tr>
<td>Stroke in the preceding 3 months</td>
<td>May be harmful; ICH potential (B)</td>
</tr>
<tr>
<td>Blood Glucose &lt; 50 mg/dL</td>
<td>Not for nonvascular issues (B)</td>
</tr>
<tr>
<td>Examples removed for BP</td>
<td>Safe when BP &lt; 185/110 (B)</td>
</tr>
<tr>
<td>Examples removed for coagulopathy</td>
<td>Not recommended/harmful (B/C)</td>
</tr>
<tr>
<td>Symptoms suggestive of SAH</td>
<td>Contraindicated (C)</td>
</tr>
<tr>
<td>History of ICH</td>
<td>Potentially harmful (C)</td>
</tr>
<tr>
<td>Arterial puncture at non-compressible site in previous 7 days</td>
<td>Uncertain (C)</td>
</tr>
</tbody>
</table>

Key takeaways

- Key Takeaway #1
  - The alteplase package insert and the AHA/ASA guidelines for alteplase use in stroke have significant differences

- Key Takeaway #2
  - The 2015 AHA/ASA evidence statement for alteplase inclusion and exclusion criteria is a great resource

- Key Takeaway #3
  - Address any issues in your institution early
References

Fosfomycin: You CAN teach an old drug new tricks

Ashley Niemczyk, PharmD, BCPS
Emergency Medicine Pharmacist
Fairview Ridges Hospital
Burnsville, Minnesota
Learning Objectives

- Review pharmacology of fosfomycin
- Describe the potential place in therapy for fosfomycin
- Understand the role fosfomycin may play in preventing admissions for ED patients
Meet AB

- 49 year old female presents to the ED
  - Increased urinary frequency, urgency, dysuria
- PMH: HTN, fibromyalgia, depression
- Objective data:
  - HR: 75 bpm
  - BP 124/74 mmHg
  - Temp: 98.4°F
  - UA: (+) nitrite, moderate leukocyte esterase, bacteria
## Meet AB

<table>
<thead>
<tr>
<th>Drug Allergy/Intolerance</th>
<th>Reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphotericin B</td>
<td>Unknown</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>Hives</td>
</tr>
<tr>
<td>Aztreonam</td>
<td>Leukopenia</td>
</tr>
<tr>
<td>Cefdinir</td>
<td>Hives</td>
</tr>
<tr>
<td>Cephalexin</td>
<td>Hives</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>Burning sensation of face</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>Weakness/dystonia</td>
</tr>
<tr>
<td>Nitrofurantoin mononitrate</td>
<td>Rash</td>
</tr>
<tr>
<td>Penicillins</td>
<td>Respiratory/rash/hives</td>
</tr>
<tr>
<td>Sulfa</td>
<td>Respiratory/rash/hives</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>Rash/swelling</td>
</tr>
</tbody>
</table>
Meet AB

You get this call from one of your ED residents:

- “Hi Ashley, I’m calling about a patient with a complex allergy history who has a UTI. We think we’re going to have to admit her for IV antibiotics.”

- How many of you have gotten this type of call??
Fosfomycin Pharmacology

- **Mechanism of Action**
  - Inhibits bacterial cell wall synthesis
  - Decreases bacterial adherence to uroepithelial cells

- **Dosing**
  - 3 g mixed in 3-4 ounces of water PO once

- **Uses**
  - Uncomplicated urinary tract infection
  - ESBL UTI?

- **Spectrum of Activity**
  - E.coli, P.mirabilis, K.pneumoniae, Enterobacter, Citrobacter, Serratia, MSSA/MRSA, VRE


Fosfomycin Hypersensitivity

- Fosfomycin structure not related to other antimicrobials
- Very few case reports reporting anaphylaxis with fosfomycin
  - No cases in patients with previously noted drug allergies

Back to AB...

- AB was given the dose of fosfomycin 3 g PO once in the ED
- Monitored and discussed signs and symptoms of allergic reaction
- Discharged to home

- ADMISSION PREVENTED!!!
Meet YZ

- 67 year old female sent to ED from clinic
  - IV antibiotics for ESBL UTI
  - Anxious and tearful about pending admission

PMH: HTN, atrial fibrillation, hyperlipidemia, DM II

Objective data:
- HR: 86 bpm
- BP: 136/82 mmHg
- Temp: 99.2°F
- Urine culture: ESBL E.coli
Meet YZ

- You get a call from the attending...
  - “Hey Ash, we have this patient who we’re admitting for ESBL E.coli UTI. What ‘penem’ would you like to use?”

- How many of you have gotten this call?
## Fosfomycin for ESBL UTI

<table>
<thead>
<tr>
<th>Study</th>
<th>ESBL Isolates (N)</th>
<th>ESBL Isolates Susceptible to Fosfomycin (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sabharwal, 2015</td>
<td>78 ((E. coli + K. pneumoniae))</td>
<td>95</td>
</tr>
<tr>
<td>Yeganeh-Sefidan, 2016</td>
<td>75 ((E. coli + K. pneumoniae))</td>
<td>97.3</td>
</tr>
</tbody>
</table>


Fosfomycin for ESBL UTI

- Systematic review

<table>
<thead>
<tr>
<th>Bacteria</th>
<th>Median ESBL Isolates N (range)</th>
<th>Median ESBL Isolates Susceptible to Fosfomycin Range (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>E.coli</td>
<td>272 (42-6644)</td>
<td>95 (81-100)</td>
</tr>
<tr>
<td>Klebsiella</td>
<td>63 (28-509)</td>
<td>63 (46.0-94.7)</td>
</tr>
<tr>
<td>Proteus</td>
<td>50 (32-85)</td>
<td>50 (50-72)</td>
</tr>
</tbody>
</table>

# Fosfomycin for ESBL UTI

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients with ESBL Isolates (N)</th>
<th>Doses of Fosfomycin (mean)</th>
<th>Cure Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sastry, 2015</td>
<td>7</td>
<td>1-3</td>
<td>71.4</td>
</tr>
<tr>
<td>Seroy, 2016</td>
<td>20 (E.coli)</td>
<td>3</td>
<td>75</td>
</tr>
<tr>
<td></td>
<td>8 (K.pneumoniae)</td>
<td>4.6</td>
<td>62</td>
</tr>
<tr>
<td></td>
<td>6 (P.mirabilis)</td>
<td>2</td>
<td>100</td>
</tr>
</tbody>
</table>


Back to YZ...

- Received one dose of fosfomycin in the ED
- Discharged with two additional doses of fosfomycin to take every 48 hours
- Follow up in ID clinic one week later showed resolution of symptoms and a clean UA

- ADMISSION PREVENTED!!
Key Takeaways

- **Key Takeaway #1**
  - Fosfomycin may be an option for patients with multiple drug allergies

- **Key Takeaway #2**
  - Multiple-dose regimen of fosfomycin has been effective in treating ESBL UTI’s

- **Key Takeaway #3**
  - Proper selection of fosfomycin use may preserve its activity while preventing admissions
Is There Additional Risk of Thrombolytic Therapy During Pregnancy?

Eric Kanouse, Pharm.D.
Emergency Medicine Clinical Staff Pharmacist
University of Rochester Medical Center
Rochester, NY
Objective

- Describe the available evidence surrounding the use of thrombolytic therapy during pregnancy
I can’t breathe...

- 28 year-old female presents with dyspnea, pleuritic pain and cough
- Vitals:
  - Temp: 38.5°C
  - HR: 110 bpm
  - BP: 80/48 mm Hg
  - RR: 30 bpm
- PMH – 16 weeks pregnant
- EM physician orders:
  - STAT Chest CT
Thrombolysis

- **Indications:**
  - Stroke
  - Pulmonary Embolism (PE)
  - Myocardial infarction

- **Adverse events:**
  - Hemorrhage
Pregnancy Considerations

- Hypercoagulable state
- Risk/benefit of thrombolytic to fetus and mother
  - Factors that influence drug entry into placenta
- American College of Chest Physicians:
  - “The use of thrombolytic therapy is best reserved for life-threatening maternal thromboembolism”
- Quality of evidence?

N = 69 patients
(case reports and series, GA 1 week – 37 week)

- Stroke, n = 18
  - Systemic, n = 12
  - Directed, n = 6

- PE, n = 27
  - Systemic, n = 24
  - Directed, n = 3

- Cardiac conditions, n = 24
  - Systemic, n = 24
  - Directed, n = 0

Safety?
**Stroke**  
(n=18)  
- Major maternal complication ~ 6%  
- Minor maternal complication ~ 22%  
- Fetal complication ~ 22%

**PE**  
(n=27)  
- Major maternal complication ~ 4%  
- Minor maternal complication ~ 15%  
- Fetal complication ~ 4%

**Cardiac Conditions**  
(n=24)  
- Major maternal complication ~ 17%  
- Minor maternal complication ~ 8%  
- Fetal complication ~ 21%

**Overall:**  
(N=69)  
- Major maternal complication ~ 9%  
- Minor maternal complication ~ 14%  
- Fetal complication ~ 14%
Key Takeaways

- Inclusion/exclusion criteria assessment
- Complication rate appears to be higher in pregnancy based on reviewed case reports and series
  - Carefully evaluate risk vs. benefit
  - Interdisciplinary approach warranted
Some Like it Hot!
Capsaicin for Cannabinoid Hyperemesis Syndrome

Daniel Paley, Pharm.D.
Emergency Medicine Clinical Pharmacist
Mercy Hospital – part of Allina Health
Coon Rapids, MN
Learning Objectives

- Describe common findings in cannabinoid hyperemesis syndrome (CHS).

- Understand the role of capsaicin in treating CHS.
Cannabinoid Hyperemesis Syndrome

- Cyclic episodes of nausea, vomiting, and epigastric pain associated with chronic marijuana use.


Look for:

Morning symptoms  Long-term history of cannabis use  Compulsive bathing
CHS: Coming to a State Near You?

[Map showing states with medical use legalization, recreational and medical use legalization, medical use on November ballot, and no legislation.]

Extra Spicy: A New Therapy for CHS

Capsaicin 0.025% - 0.075% cream applied directly to the abdomen, arms, and/or back.

Relief of nausea, vomiting, and GI pain within 30 minutes.

Biary R at al. Clinical Toxicology 2014; 52: 787
Lapoint J. Clinical Toxicology 2014; 52: 707
**Capsaicin Mechanism of Action**

- **Activators of TRPV1**
  - Capsaicin
  - Endogenous agonists
  - Acidosis
  - Heat
  - $\text{H}^+$
  - $\text{Na}^+$
  - $\text{Ca}^{2+}$

- Neuronal membrane
- Depolarization and action potential initiation
- Localized defunctionalization
- $\text{Ca}^{2+}$ overload, mitochondrial dysfunction, etc.

- Brain: burning, stinging, or itching sensations

### Evidence

<table>
<thead>
<tr>
<th>Abstract (1)</th>
<th>Abstract (2)</th>
<th>Poster (3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NACCT 2014</td>
<td>NACCT 2014</td>
<td>ACMT 2016</td>
</tr>
<tr>
<td>- N=5</td>
<td>- N=1</td>
<td>- N=3</td>
</tr>
<tr>
<td>- 0.075% cream</td>
<td>- 0.025% cream</td>
<td>- 0.075% cream</td>
</tr>
<tr>
<td>- Success</td>
<td>- Success</td>
<td>- Success</td>
</tr>
</tbody>
</table>

1. Lapoint J. Clinical Toxicology 2014; 52: 707
2. Biary R et al. Clinical Toxicology 2014; 52: 787
Key Takeaways

- Cannabinoid hyperemesis syndrome is characterized by vomiting associated with heavy and long-term marijuana use.

- Clues: marijuana use history, compulsory showering behavior.

- Capsaicin cream applied to the abdomen/back/arms can relieve symptoms within 30 minutes.
Tweet Your Questions

@PharmERToxGuy

Q & A Part 3
(True or False) The use of succinylcholine leads to a significant increase in ICP, which then increases mortality, in all patients with TBI.

A  TRUE
B  FALSE
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A  TRUE
B  FALSE
Question

Of the following contraindications removed or amended in the PI, which has the highest rated evidence to support it as an exclusion criteria for alteplase in stroke?

- A. Arterial puncture at non-compressible site in previous 7 days
- B. Previous stroke in preceding 3 months
- C. History of ICH
- D. Symptoms of SAH
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Use fosfomycin with caution in patients with which drug allergy?

A. Penicillins
B. Sulfa
C. Tetracyclines
D. None of the above
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B. Review contraindications to thrombolytic therapy
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Which of the following characteristics of CHS is NOT correct?

- **A** Occurs only in teenaged marijuana users
- **B** Associated with heavy marijuana use
- **C** Morning predominance of symptoms
- **D** Relieved by hot showers
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Emergency Medicine Pearls

Section Advisory Group on Emergency Care
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American Society of Health-System Pharmacists (ASHP)