We Didn't Start the Fire:
Hot Topics in Emergency Medicine

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Conflicts of interest

- Jaxson Burkins has no actual or potential conflicts of interest
- Giles Slocum has no actual or potential conflicts of interest

Learning objectives

Pharmacists

1. Compare risks and benefits of emerging medication therapies in the emergency department
2. Describe appropriate administration and counseling points for unique medications in emergent situations

Pharmacy Technicians

1. Identify medications necessitating urgent preparation and delivery in emergency situations
2. Describe the unique indications of select medications being administered in the emergency department

Hot topics to be addressed today

- Emergency medicine current practice is becoming challenged
  - Ceiling effects of ibuprofen and ketorolac for acute pain
  - Role of glucagon in esophageal foreign body impaction
  - Adenosine mixture and administration technique
- Historical medications coming back to forefront
  - Droperidol returns
  - Capsaicin for cannabinoid hyperemesis syndrome
  - Ketamine for acute pain
  - Lidocaine for pain associated with kidney stones

Challenging the current practice in the emergency department

Ketorolac

- Ketorolac is one of the most commonly used injectable medications in the emergency department for pain management
- Can be injected intravenously (IV) or intramuscularly (IM)
- Also contains antipyretic and anti-inflammatory properties

Traditional dosing

- Pediatric
  - 0.5 mg/kg/dose every 6 to 8 hours (max 30 mg/dose)
  - Not to exceed 5 days
- Adult
  - IM: 60 mg x1, or 30 mg every 6 hours (max 120 mg/day)
  - IV: 30 mg x1, or 30 mg every 6 hours (max 120 mg/day)
  - Not to exceed 5 days
- Of note, there is oral ketorolac
  - not included in this presentation

Motov S, et al. Ann Emerg Med. 2017 Aug;70(2):177-184.

Adverse effects

- Gastrointestinal hemorrhage
- Nausea and vomiting
- Dyspepsia
- Dizziness and/or lightheadedness
- Evidence for platelet aggregation inhibition
- **5 day limit!**
- However, several studies have noted that we are dosing ketorolac too high!

Motov S, et al. Ann Emerg Med. 2017 Aug;70(2):177-184.

Is there a ceiling effect to ketorolac?

- Randomized, double-blind trial at a single center, with the goal of determining if ketorolac 10 mg IV for treatment of acute pain is the same as with 15 and 30 mg IV
- Inclusion
  - Adults 18 to 65 years of age presenting to the ED for acute pain (>5 on 1 to 10 pain scale) that had an onset within 30 days or less
- Excluded
  - Pregnant or breastfeeding, active GI ulcer or hemorrhage, unstable vital signs, kidney or liver impairment, or patients having already received a pain medication.

Motov S, et al. Ann Emerg Med. 2017 Aug;70(2):177-184.

How did they conduct the study?

- The EM pharmacist prepared the dose (10, 15, or 30 mg) in 10 mL of 0.9% sodium chloride and blinded to the physician, nurse, and patient
- Pain scores, vital signs, and adverse effects were logged
  - Baseline, 15, 30, 60, 90 and 120 minutes
- If patient still required pain medications at 30 minutes, a rescue agent was offered
- Outcomes
  - Primary: Reduction in numeric rating scale pain score at 30 minutes
  - Secondary: rates and percentages of patients experiencing adverse effects and requiring rescue analgesia

Motov S, et al. Ann Emerg Med. 2017 Aug;70(2):177-184.

Results

- 240 patients enrolled (80 in each group [10, 15, 30 mg])

Primary outcome	10 mg	15 mg	30 mg
Reduction in pain score at 30 minutes	Baseline 7.7 to 5.2 (difference 2.5)	Baseline 7.5 to 5.1 (difference 2.4)	Baseline 7.8 to 4.8 (difference 3.0)

- Secondary outcome
  - There were no differences between the groups and rescue analgesia at any time
  - There were no clinically significant adverse effects related to the study medication at any dose
    - Dizziness, nausea, and headache being most common

Motov S, et al. Ann Emerg Med. 2017 Aug;70(2):177-184.

Future direction

- Limitations
  - Single center, enrolled as convenience sample
  - Duration of study may have been inadequate to identify more severe adverse events
  - 30 minutes may not have been long enough for ketorolac to work
  - Vial sizes are 15 mg/mL – 15 mg may be easier to provide in many EDs
- Can we extrapolate this intramuscular doses for acute pain?

Motov S, et al. Ann Emerg Med. 2017 Aug;70(2):177-184.

Ceiling effect ketorolac

Have you already started to dose reduce your ketorolac at your institution?

- Yes
- No
- Maybe?

Food stuck in your esophagus?

- Esophageal foreign body impaction (EFBI) may result in inability tolerate anything orally, impact the airway, and possibly tear the esophagus
- Most pass on their own, some may require emergent intervention to clear the foreign body
- If a medication works, the provider wants to avoid that emergent intervention

Peksa GD, et al. Pharmacotherapy. 2019 Apr;39(4):463-472
By de:Benutzer:Mond76 - Own work, Public Domain, https://commons.wikimedia.org/w/index.php?curid=674682

Food stuck in your esophagus?

- Glucagon
  - 0.5-1 mg IV push x1, followed by 1 mg if needed
- Goal
  - Increase peristalsis
  - Relax lower esophageal sphincter
- American Society for Gastrointestinal Endoscopy
  - Recommends glucagon as intervention

Peksa GD, et al. Pharmacotherapy. 2019 Apr;39(4):463-472
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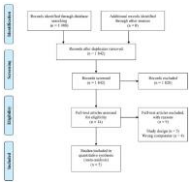
Systematic review and meta-analysis

- All retrospective, prospective, observational, and randomized controlled trials assessing glucagon for the relief of acute EFBI were included
- 1842 studies were identified, abstracts were reviewed leaving 14 articles for full-text review
- 5 studies ultimately used with 1185 total patients



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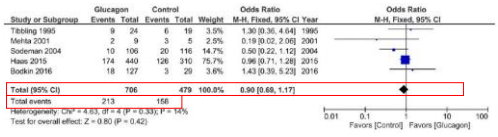
Peksa GD, et al. Pharmacotherapy. 2019 Apr;39(4):463-472

SRMA: Primary outcome – Treatment success



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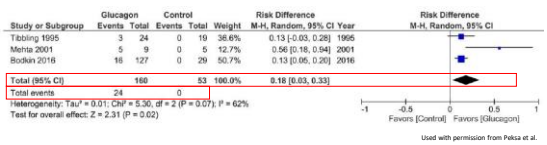
Peksa GD, et al. Pharmacotherapy. 2019 Apr;39(4):463-472

SRMA: Secondary outcome – Adverse events



Used with permission from Peksa et al.

Adverse events including vomiting and retching, burning sensations, hiccups, and chest pain

Peksa GD, et al. Pharmacotherapy. 2019 Apr;39(4):463-472

Future direction

- Glucagon did not result in improved rates of treatment success, yet also resulted in higher rates of adverse events as compared with a control group
- Literature is lacking a true cost analysis
- Maybe a role for benzodiazepines, nitroglycerin, or carbonated beverages?
  - Anyone up for a randomized controlled trial?
- Or just cut straight to gastrointestinal intervention?

Peksa GD, et al. Pharmacotherapy. 2019 Apr;39(4):463-472

Going from 140 (bpm) to 80 (bpm) in seconds

- Supraventricular tachycardia (SVT) includes:
  - Atrial fibrillation, atrial flutter, sinus tachycardia, etc.
- Accounts for up to 50,000 ED visits annually
- Can be life threatening

McDowell M, et al. Acad Emerg Med. 2020 Jan;27(1):61-63
Photo credit: www.pixabay.com

Going from 140 (bpm) to 80 (bpm) in seconds

- American Heart Association 2015 Guidelines for Advanced Cardiac Life Support
  - Stable, regular complex, narrow-complex, SVT
  - **Adenosine!** (Class IIb, LOE C)
- Mechanism of action
  - Atrial/Ventricle node blocker
- Onset = Rapid; Duration = Very brief
- Goal: Chemically converting SVT

McDowell M, et al. Acad Emerg Med. 2020 Jan;27(1):61-63
Photo credit: www.pixabay.com

Adenosine

- Dose
  - 6 mg rapid IV push x1, followed by 12 mg rapid IV push
  - Start with 3 mg if:
    - Meds
    - Transplant/central line
- Administration
  - Traditionally, two syringes with stopcock
- Potential problems
  - Locating stopcock, precise coordination of delivering and flushing simultaneously

McDowell M, et al. Acad Emerg Med. 2020 Jan;27(1):61-63

Single-syringe dose of diluted adenosine

- This single-center, prospective, observational study was conducted from November, 1, 2016, through February 28, 2018
- Only adults with stable narrow-complex tachycardia requiring adenosine included
- Open label trial
  - Physician would request their preferred adenosine administration method
  - EM pharmacist would prepare either
    - 6 mg adenosine and 18 mL of 0.9% sodium chloride combined in single syringe
    - 6 mg adenosine and 20 mL of 0.9% sodium chloride in two syringes

McDowell M, et al. Acad Emerg Med. 2020 Jan;27(1):61-63

Administration techniques

Single Syringe

Two Syringes

Outcomes

Primary outcome	Single Syringe (n=26)	Two Syringe (n=27)	P value
Conversion to NSR after 1 dose	73.1% (95% CI 0.55-0.91)	40.7% (95% CI 0.21-0.61)	0.0176

Secondary outcome	Single Syringe (n=26)	Two Syringe (n=27)	P value
Conversion to NSR after up to 3 doses	100% (95% CI 1.0-1.0)	70.4% (95% CI 0.52-0.0.89)	0.0043

NSR – Normal sinus rhythm, CI – confidence interval

McDowell M, et al. Acad Emerg Med. 2020 Jan;27(1):61-63

Safety and limitations

- Safety
  - Single syringe: no adverse events documented
  - Two syringes: 1 patient experience extravasation and phlebitis
- Limitations
  - Not powered – did not meet goal of 75 patients per arm
  - Not randomized
  - No documentation of location of IV access (distance drug travels may impact result)
  - Patients could have received additional rate controlling medications prior to adenosine

McDowell M, et al. Acad Emerg Med. 2020 Jan;27(1):61-63

2020 ICHP Annual Meeting OUR TEAM CAN

Future direction

- While adenosine mixed in a single syringe looks promising, a randomized controlled trial will be necessary to confirm what this pilot study showed

McDowell M, et al. Acad Emerg Med. 2020 Jan;27(1):61-63

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What medication can be mixed in a single syringe in the patient's room for immediate administration to stop a very fast, stable, heart rate? (technician assessment)

A. Ibuprofen
B. Ketorolac
C. Adenosine
D. Glucagon

What adverse effect is most common when administering glucagon for esophageal foreign body impaction? (pharmacist assessment)

A. Hypotension
B. Rash
C. Diarrhea
D. Vomiting

Seasoned medications making a resurgence

Droperidol is baaaack

- Dopamine antagonist
- Properties
  - Analgesic, Sedative, Antiemetic
  - Rapid Onset
  - Administered Intramuscular or Intravenous
- Indications
  - Post-Operative Nausea & Vomiting (0.625 – 1.25 mg)
  - *Off-Label: Acute Agitation (2.5 – 10 mg), Migraines (1.25 – 2.5 mg)*

Droperidol [package insert]. Shirley, NY. American Regent, Inc. 2019.

Droperidol is baaaack

BLACK BOX WARNING
QT prolongation and Torsade de Pointes

- 2001 FDA Recommendations
  - 12-Lead ECG prior to administration
  - ECG monitoring 2-3 hours post-administration
  - Doses > 2.5 mg
- Significant scrutiny on Black Box Warning
- Utilization decreased, production ceased
- 2019 Returned to market

Droperidol [package insert]. Shirley, NY. American Regent, Inc. 2019.

Droperidol is baaaack

- Is it safe?
  - Fatalities – 0%
  - Fatal arrhythmias – 2.9%
  - Akathisia – 2.9%
- Is it effective?

	n	Rescue Medications, n (%)
Pain	1387	102 (7.4)
Headache	3622	188 (5.2)
Sedation	599	0
Nausea/Vomiting	856	0

Gaw CM, et al. Am J Emerg Med. 2019. pii:S0735-6757(19)30612-6

Legalized cannabis is making me sick

- What is cannabinoid hyperemesis syndrome (CHS)?
  - Cyclic & recurrent
  - Nausea, vomiting, abdominal pain
  - High-frequency & extended duration marijuana use
- Current management options
  - Anti-emetics? Antipsychotics?
    - Often ineffective
  - Hot showers?
    - Often effective, but temporary
  - Capsaicin?
    - Mechanism: transient receptor potential vanilloid 1 (TRPV1) agonist

Wagner S, et al. Clin Toxicol (Phila). 2019 Sep 4:1.
Cruz A, et al. Clin Toxicol (Phila). 2020 Jan 8:1.

Legalized cannabis is making me sick

- Mechanism
  - Not fully understood
  - Transient receptor potential vanilloid 1 (TRPV1) agonist
    - Also activated by heat stimuli
  - Chronic use of cannabinoids downregulates TRPV1 receptor
  - Stimulation of TRPV1 alleviates GI symptoms
- Administration
  - Clean, dry area of abdomen
  - 1-mm-thick coating
  - Wear gloves when applying
- Rapid Onset (5-10 minutes)

Wagner S, et al. Clin Toxicol (Phila). 2019 Sep 4:1.
Cruz A, et al. Clin Toxicol (Phila). 2020 Jan 8:1.

Legalized cannabis is making me sick

Topical Capsaicin – does it work?

- Retrospective cohort analysis
- n=43

	Capsaicin	No capsaicin	p
Median ED Length of Stay	179 minutes	201 minutes	0.33
Rescue therapies	3	4	0.015
Adverse events	--	--	N/A
Opioid usage	69 mg OME	166.5 OME	--

OME: Oral Morphine Equivalent

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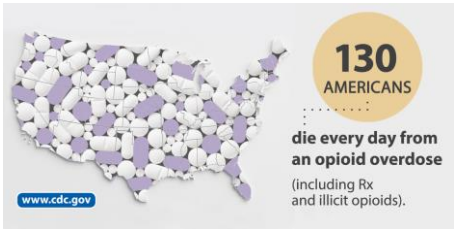
Cruz A, et al. Clin Toxicol (Phila). 2020 Jan 8:1.

Opioid alternatives?



Opioid alternative? Ketamine for acute pain

- "Low Dose Ketamine"
- Systematic Review and Meta-analysis
- Randomized controlled trials compared IV opioids to low-dose ketamine (n=3)

Pain scale reduction with ketamine non-inferior to IV morphine.

Karlow N, et al. Acad Emerg Med. 2018 Oct. 25: 1086-97.

Opioid alternative? Ketamine for acute pain

	Ketamine
Dose	0.3 mg/kg IV (Typical max 30 mg) 0.5 – 1.0 mg/kg Intranasal
Administration	SLOW IV Push (5 minutes) OR *Short Infusion (in 100 mL bag over 15 min)
Adverse Effects	- Hypertension - Hallucinations, dizziness - Unreality
Ideal Patient Population	- Chronic opioid use - In detox program - Concern for respiratory depression

Karlow N, et al. Acad Emerg Med. 2018 Oct. 25: 1086-97.

Another opioid alternative? Lidocaine too

- Systematic Review
- Randomized controlled trials (n=13)
- Compared IV lidocaine to various agents
  - IV morphine, IV ketorolac, IV dihydroergotamine (DHE), IV chlorpromazine
- Stratifying based on sources of pain
  - IV lidocaine > morphine for renal colic and critical limb ischemia
  - IV lidocaine > DHE for migraine
  - IV lidocaine = ketorolac for lower back pain
  - IV lidocaine < chlorpromazine for migraine

Makhoul T, et al. Am J Emerg Med. 2019 Apr. 37:775.
Masic D, et al. Pharmacotherapy. 2018 Dec. 38:1250-1259.

Opioid alternative?

	Ketamine	Lidocaine
Dose	0.3 mg/kg IV (Typical max 30 mg) 0.5 – 1.0 mg/kg Intranasal	1.5 mg/kg IV (Typical max 150 mg)
Administration	SLOW IV Push (5 minutes) OR *Short Infusion (in 100 mL bag over 15 min)	Short infusion (in 100 mL bag over 15 min)
Adverse Effects	- Hypertension - Hallucinations, dizziness - Unreality	- Headache
Ideal Patient Population	- Chronic opioid use - In detox program - Concern for respiratory depression	- Chronic Opioid Use - In detox program - Acute Renal Colic

Makhoul T, et al. Am J Emerg Med. 2019 Apr. 37:775.
Masic D, et al. Pharmacotherapy. 2018 Dec. 38:1250-1259.
Karlow N, et al. Acad Emerg Med. 2018 Oct. 25. 1088-97.

Illinois pharmacists making a difference!

- You may have noticed some familiar names on these studies…
- Many of the studies reviewed in this presentation contained authorship from pharmacists practicing in Illinois!

Which of the following contains a Black Box Warning for risk of QT prolongation and Torsades de Pointes?

A. Capsaicin
B. Droperidol
C. Ketamine
D. Lidocaine

Which of the following adverse effects occurs when Ketamine is administered too rapidly?

A. Headache
B. Hypertension
C. Nausea
D. Unreality

References

Motov S, et al. Comparison of Intravenous Ketorolac at Three Single-Dose Regimens for Treating Acute Pain in the Emergency Department: A Randomized Controlled Trial. Ann Emerg Med. 2017 Aug;70(2):177-184.

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