Non-Opioid Pain Management: In the ED and Beyond

Craig P. Worby, PharmD BCCCP BCPS
Clinical Lead Pharmacist – Emergency Medicine
Dartmouth Hitchcock Medical Center

Objectives

- Describe the pathophysiology of pain
- Compare and contrast alternatives to opioids for pain management
- Analyze supporting literature for non-opioid pain options
- Recommend appropriate medication therapy given a patient case

What is Covered

- Strategies and approaches to acute pain in ED
- Paradigm shifts in perceptions of pain management
- New data on combination therapy of acetaminophen + ibuprofen
- New data on ketorolac
- Ketamine
- Intravenous lidocaine

What is Not Covered

- ICU Pain Management
- Neuropathic Pain
- Chronic Pain
- Cancer Pain

Epidemiology

- 33,091 overdose deaths involving an opioid in 2015
- ED only accounts for 4.7% of opioid prescriptions, but is frequently where patients are first introduced to opioids
- Percentage of ED visits in which an opioid is prescribed rose from 20.8% in 2001 to 31.0% in 2010
- 17% of patient's prescribed an opioid for acute pain were still taking the medication 1 year after initial ED visit

Red Flags for Opioid Abuse Potential

- Adolescents and young adults
- History of substance use (including tobacco)
- Social isolation or dysfunction
- Existing psychiatric disease
- Concomitant use of sedatives

PHYSIOLOGY OF PAIN

5 PHASES OF ADAPTIVE PAIN

TRANSDUCTION
CONDUCTION
TRANMISSION
PERCEPTION
MODULATION

NMDA RECEPTORS
OPIOID RECEPTORS

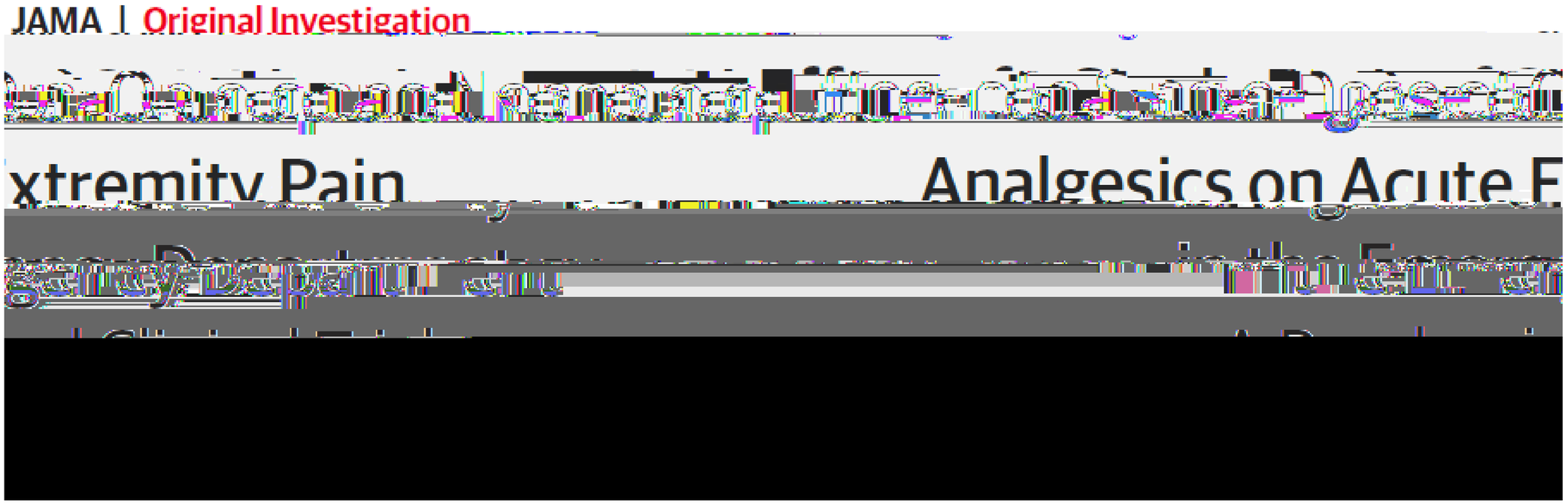
NA+ CHANNELS

Acetaminophen + Ibuprofen

- Possible synergistic effect by decreasing pain through multiple mechanisms
- Combination used in Australia, New Zealand, and Europe
- Limited data to date – postoperative and dental pain

- Advantages
  - Cost-effective
  - Limited adverse effects
- Disadvantages
  - Perception & guidance

Hot off the Press



Non-Opioid vs. Opioid Extremity Pain

- Patients aged 21 to 64 presenting to ED with acute extremity pain
- Randomized, double-blind, treatment control
- 4 intervention groups
  - 400 mg ibuprofen + 1000 mg acetaminophen
  - 5 mg oxycodone + 325 mg acetaminophen
  - 5 mg hydrocodone + 325 mg acetaminophen
  - 30 mg codeine + 325 mg acetaminophen
- Primary: NRS pain score at 2 hours
- Secondary:
  - NRS pain score at 1 hour
  - Severity of pain – none, mild, moderate, severe

Chang AK, etal. JAMA. 2017

Non-Opioid vs. Opioid Extremity Pain

- 411 patients enrolled
  - 101 patients – APAP + ibuprofen
  - 104 patients – oxycodone + APAP
  - 103 patients – hydrocodone + APAP
  - 103 patients – codeine + APAP
- Notable demographics
  - 60% latino, 31% black
  - 62% presented with muscle strain or sprain
  - 22% presented with extremity fracture

Chang AK, etal. JAMA. 2017

Non-Opioid vs. Opioid Extremity Pain

Chang AK, etal. JAMA. 2017

- 17.8% of patients received rescue analgesia
  - Predominantly oxycodone

PAIN MANAGEMENT

KETOROLAC

- Patients aged 18-65 presenting to ED with acute flank,

Ketorolac Dosing in ED

- 240 patients enrolled
  - 80 patients received 10 mg
  - 80 patients received 15 mg
  - 80 patients received 30 mg
- Notable demographics
  - 45% male
  - 38% abdominal pain, 33% flank pain, 24% musculoskeletal pain

Motov S, etal. Ann Emerg Med. 2017

PAIN MANAGEMENT

KETAMINE

Ketamine

- Studied uses:
  - Acute pain – wide range of etiologies
  - Chronic pain
- Studied routes
  - IV, IM, Intranasal, SubQ

- Dosing
  - Subdissociative: 0.15 – 0.6 mg/kg IV bolus
    - Consider mixing in 50 mL NS and administer over 15 minutes (Motov, 2017)
  - Anesthetic: 1-4.5 mg/kg
- Duration of Effect
  - Peak at 15 minutes
  - May last up to 1-2 hours

- Advantages
  - Large therapeutic window
  - Lack of respiratory depression
- Disadvantages
  - Limited data – small trials in ED and postoperative setting
  -

Ketamine Adverse Effects

Subdissociative Dosing	Anesthetic Dosing
Nausea	Hypertension
Dizziness	Tachycardia
Feeling of unreality	Emergence reactions
Hallucination - rare	Elevated intraocular pressures
Mild elevations in blood pressure	Elevations in intracranial pressures?

Avoid Ketamine

- Psychiatric illness
- Systolic blood pressure > 180 mmHg
- Heart rate > 150 beats per minute

- Patients aged 18-55 presenting to ED with acute abdominal, flank, back, or musculoskeletal pain with a NRS > 5
- Prospective, randomized, double-blind
- 2 intervention groups
  - Ketamine 0.3 mg/kg
  - Morphine 0.1 mg/kg
- Primary: reductiioineaLionTc 0 TTTTTTTTTTc 0 Tw d26 >>BDC

- 90 patients enrolled
  -

Motov S, etal. Ann Emerg Med. 2015

Motov S, etal. Ann Emerg Med. 2015

Assessment Question

Which of the following patients is the best candidate for ketamine for pain?

A. 27 year old with a fractured ankle and a history of schizophrenia
B. 74 year old with back pain and a blood pressure of 170/110
C. 55 year old with a myocardial infarction
D. 46 year old with abdominal pain and a tolerance to opioids

PAIN MANAGEMENT

LIDOCAINE

Lidocaine

- Dosing:
  - Intravenous lidocaine 2% (20 mg/mL)
    - Patients should be on 1.5 mg/kg actual body weight (max: 200 mg)
    - Dilute in 100-250 mL of D5W or NS
    - Infuse over 10-20 minutes
- Telemetry during administration and monitored for bradycardia

Lidocaine

- Advantages
  - Safe and effective
  - Cost effective

- Disadvantages
  - Potential for medication errors
  - Data limited to small studies and case series
  - Indications in which most effective are limited
  - Consider telemetry monitoring with IV administration

- Common
  - Nausea, vomiting, abdominal pain
  - Dizziness
  - Perioral numbness
- Uncommon
  - Metallic taste
  - Tremor
  - Dry mouth
  -

Lidocaine IV vs. Morphine in Renal Colic

- Adults aged 18-65 years presenting to ED with renal colic
- Prospective, randomized, double blind, single center
- 2 intervention groups
  - Lidocaine IV 1.5 mg/kg
  - Morphine IV 0.1 mg/kg
- Primary: reduction in VAS at 5, 10, 15, and 30 minutes
- Secondary:

Soleimanpour H, etal. BMC Urol. 2012

Lidocaine IV vs. Morphine in Renal Colic

- 240 patients enrolled
  - 120 received lidocaine IV
  - 120 received morphine IV
- Notable demographics
  - 73% patients were male
  - Mean age 36 years old

Soleimanpour H, etal. BMC Urol. 2012

Lidocaine IV vs. Morphine in Renal Colic

Soleimanpour H, etal. BMC Urol. 2012

Lidocaine IV vs. Morphine in Renal Colic

- More patients responded to lidocaine than morphine 90% vs 70% (p=0.00001)
- Lidocaine was well tolerated, with dizziness being the most common adverse effect
- Conclusion: lidocaine is a safe an effective alternative to opioids in managing renal colic

Soleimanpour H, etal. BMC Urol. 2012

Lidocaine IV vs. Ketorolac Back Pain

- Patients aged 15-55 with acute radicular back pain
- Randomized, double-blind, single center
- 2 intervention groups
  - Lidocaine IV 100 mg
  - Ketorolac IV 30 mg
- Primary: Difference in VAS at 60 minutes
- Secondary: Patient pain relief score at 1 week

Tanen DA, etal. J Emerg Med. 2014

Lidocaine IV vs. Ketorolac Back Pain

- 41 patients enrolled
  - 21 patients received lidocaine
  - 20 patients received ketorolac
- Notable demographics
  - Mean age 37 years
  - Mean weight 88.6 kg

Tanen DA, etal. J Emerg Med. 2014

Lidocaine IV vs. Ketorolac Back Pain

- 67% of patients in the lidocaine group required rescue analgesics
- No adverse effects were tracked
- Conclusions: while lidocaine decreased radicular back pain from baseline, it did not reach clinical significance

Tanen DA, etal. J Emerg Med. 2014

Lidocaine Additional Data

Setting	Indication	N	Route	Dose	Comparator	Result	Conclusions	Reference
ED	Critical limb ischemia	63	IV	2 mg/kg	Morphine 0.1 mg/kg	At 60 minutes, lidocaine had a mean reduction of 2.25 in VAS	Lidocaine superior to morphine	Emerg Med J 2015
Meta-analysis	Neuropathic Pain	329	IV	1-5 mg/kg	placebo	Pooled analysis – reduction in VAS by 10.60 mm and superior to placebo (-10.02 mm, p=0.002)	IV lidocaine is effective compared to placebo for neuropathic pain	

Assessment Question

Which of the following is FALSE about lidocaine for pain management?

A. Intravenous lidocaine has been shown to be efficacious when administered for acute lower back pain
B. Lidocaine doses of 1.5 mg/kg (about 100 mg) have been shown to be safe with few side effects
C. Much of the data for intravenous lidocaine in the ED comes from small studies and case series

JA is a 53 year old female presenting to the ED with 9/10 pelvic pain. A CT scan reveals a new nephrolithiasis in her ureter. JA's past medical history is significant for back pain and opioid abuse (sober for 3 years). Allergies list GI bleeding with NSAID use. Home medications include: acetaminophen 1000 mg every 6 hours as needed for back pain and omeprazole 20 mg daily. Given her history, JA requests avoiding anything with the potential for addiction.

Future Directions

Key Takeaways

- Consider non-opioid analgesia first, even if moderate-severe pain
  - Acetaminophen 1000 mg + ibuprofen 400 mg
  - Ketorolac at limited doses (10 mg)
- Subdissociative ketamine is an effective alternative to opioids for pain
  - Administer over 15 minutes to reduce adverse effects
- Lidocaine is effective for renal colic and neuropathic indications but needs more research
  - While safe, recommend cardiac monitoring

Questions?

- Email: Craig.P.Worby@hitchcock.org

References

- Kyriacou DN. Opioid vs Nonopioid Acute Pain Management in the Emergency Department. JAMA. 2017;318(17):1655–1656. doi:10.1001/jama.2017.16725
- Chang AK, Bijur PE, Esses D, Barnaby DP, Baer J. Effect of a Single Dose of Oral Opioid and Nonopioid Analgesics on Acute Extremity Pain in the Emergency DepartmentA Randomized Clinical Trial. JAMA. 2017;318(17):1661–1667. doi:10.1001/jama.2017.16190
- Motov S, Yasavolian M, Likourezos A, etal. 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. doi: 10.1016/j.annemergmed.2016.10.014. Epub 2016 Dec 16.
- Motov S, Rockoff B, Cohen V, etal. Intravenous Subdissociative-Dose Ketamine Versus Morphine for Analgesia in the Emergency Department: A Randomized Controlled Trial. Ann Emerg Med. 2015 Sep;66(3):222-229.e1. doi: 10.1016/j.annemergmed.2015.03.004. Epub 2015 Mar 26.
- Motov S, Mai M, Pushkar I, etal. A prospective randomized, double-dummy trial comparing IV push low dose ketamine to short infusion of low dose ketamine for treatment of pain in the ED. Am J Emerg Med. 2017 Aug;35(8):1095-1100. doi: 10.1016/j.ajem.2017.03.004. Epub 2017 Mar 3.
- Bowers KJ, McAllister KB, Ray M, etal. Ketamine as an Adjunct to Opioids for Acute Pain in the Emergency Department: A Randomized Controlled Trial. Ketamine as an Adjunct to Opioids for Acute Pain in the Emergency Department: A Randomized Controlled Trial.
- Zitek T, Gates M, Pitotti C, etal. A Comparison of Headache Treatment in the Emergency Department: Prochlorperazine Versus Ketamine. Ann Emerg Med. 2017 Oct 13. pii: S0196-0644(17)31568-8. doi: 10.1016/j.annemergmed.2017.08.063. [Epub ahead of print]
- Farnia MR, Jalali A, Vahidi E, etal. Comparison of intranasal ketamine versus IV morphine in reducing pain in patients with renal colic. Am J Emerg Med. 2017 Mar;35(3):434-437. doi: 10.1016/j.ajem.2016.11.043. Epub 2016 Nov 22.
- Shachar Shimonovich, Roy Gigi, Amir Shapira, etal. Intranasal ketamine for acute traumatic pain in the Emergency Department: a prospective, randomized clinical trial of efficacy and safety. BMC Emerg Med. 2016; 16: 43.