Opioid stewardship and novel non-opioid approaches to safe and effective pain management

DR. BILLY SIN, PHARM.D., MBA, BCPS
ASSISTANT DIRECTOR OF PHARMACY
MOUNT SINAI QUEENS

DR. TRAN H. TRAN, PHARMD, BCPS
ASSOCIATE PROFESSOR, MIDWESTERN UNIVERSITY CHICAGO COLLEGE OF PHARMACY
SUBSTANCE USE INTERVENTION TEAM PHARMACIST, RUSH UNIVERSITY MEDICAL CENTER
CHICAGO, ILLINOIS
TTRAN@MIDWESTERN.EDU

Disclosures

Dr. Tran Tran is a subject matter expert for the Midwest ALTO pilot project as a consultant for the Illinois Hospital Association.

Dr. Billy Sin has no financial conflicts of interest

Objectives

1. Cite the major reasons for the opioid crisis
2. Identify supporting evidence for use of non-opioid alternatives
3. Describe the appropriate use of alternative to opioids for treatment of different types of pain
4. Review the implementation of an opioid-reduction process & policy

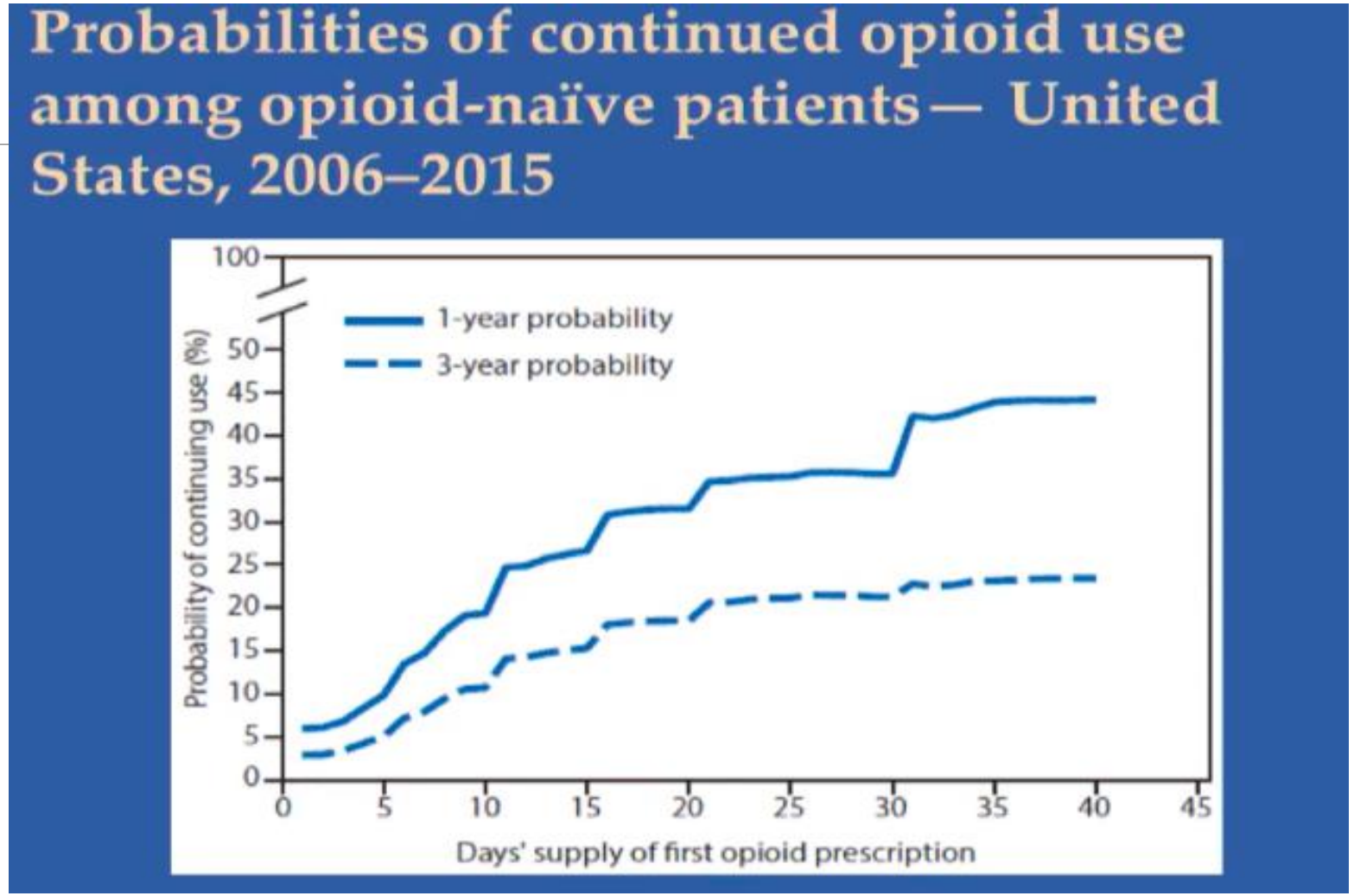
Epidemiology of the opioid crisis

HOW DID WE GET HERE?

Overemphasis of analgesia

- The pain scale and the fifth vital sign
- Purdue pharma
- Lower bar for substance abuse (drug dealer vs medicine cabinet)
- Tolerance-->larger doses-->addiction
- Cost: Rx Opioids vs Heroin
- Jails, institutions, and death

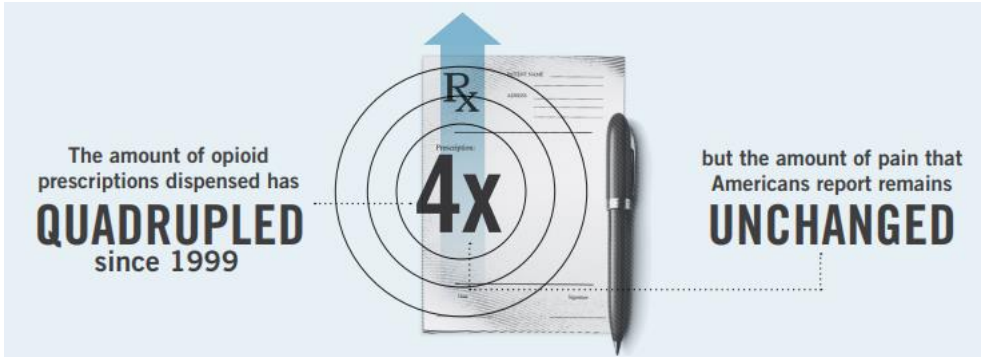
Troubling side effects



Source: Characteristics of Initial Prescription Episodes and Likelihood of Long-Term Opioid Use — United States, 2006–2015. March 2017 MMWR. Morbidity and mortality weekly report 66(10):265-269

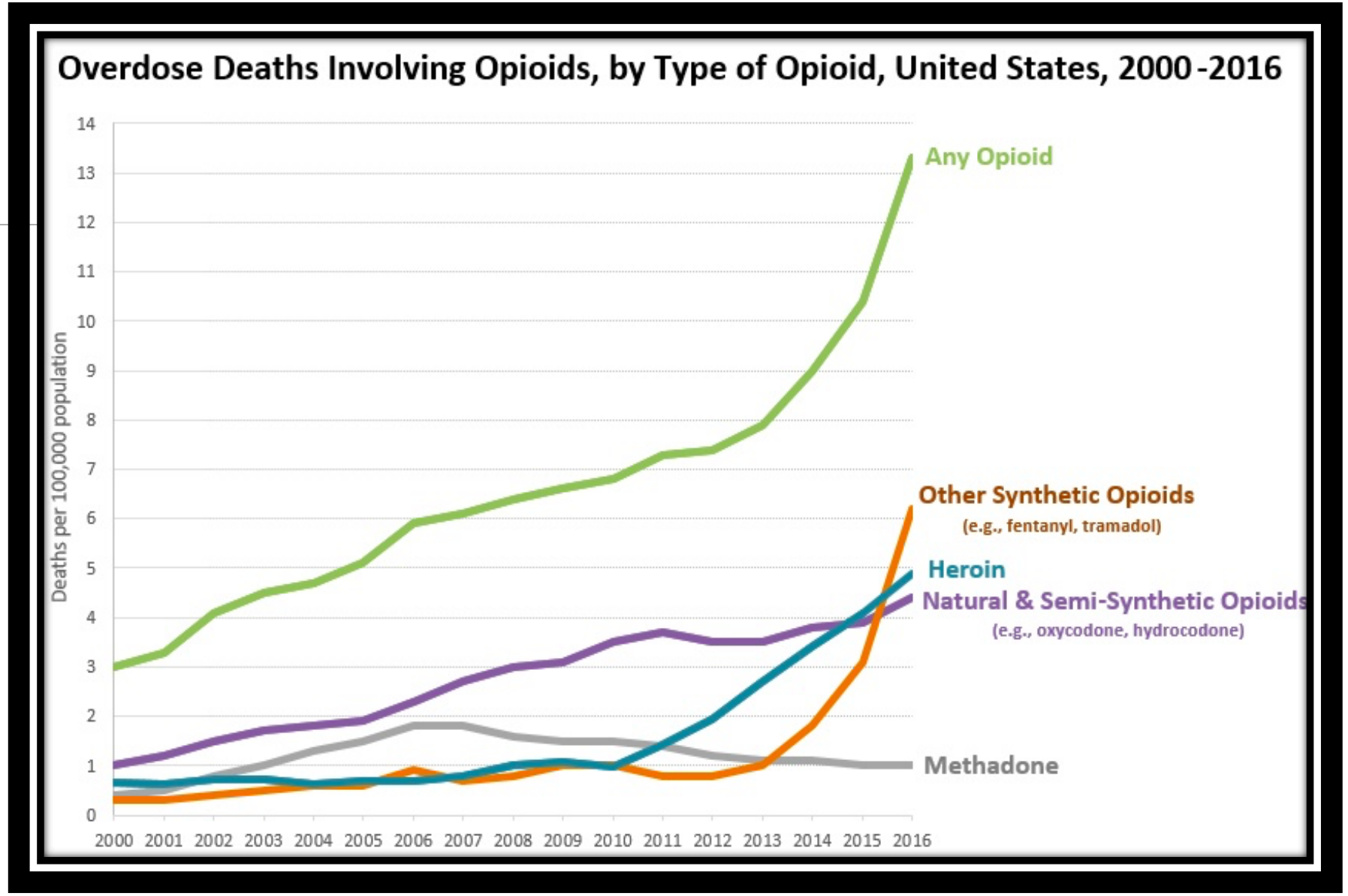
Tragic statistics

- US consumes 99% of the world's hydrocodone
- Number of annual opioid prescriptions written in the US is roughly equal to the number of adults in the country
- One of every 550 patients started on opioid therapy died of opioid-related causes a median of 2.6 years after first Rx
- 50% of opioid-related deaths are caused by opioids obtained from a family member or friend



Troubling statistics

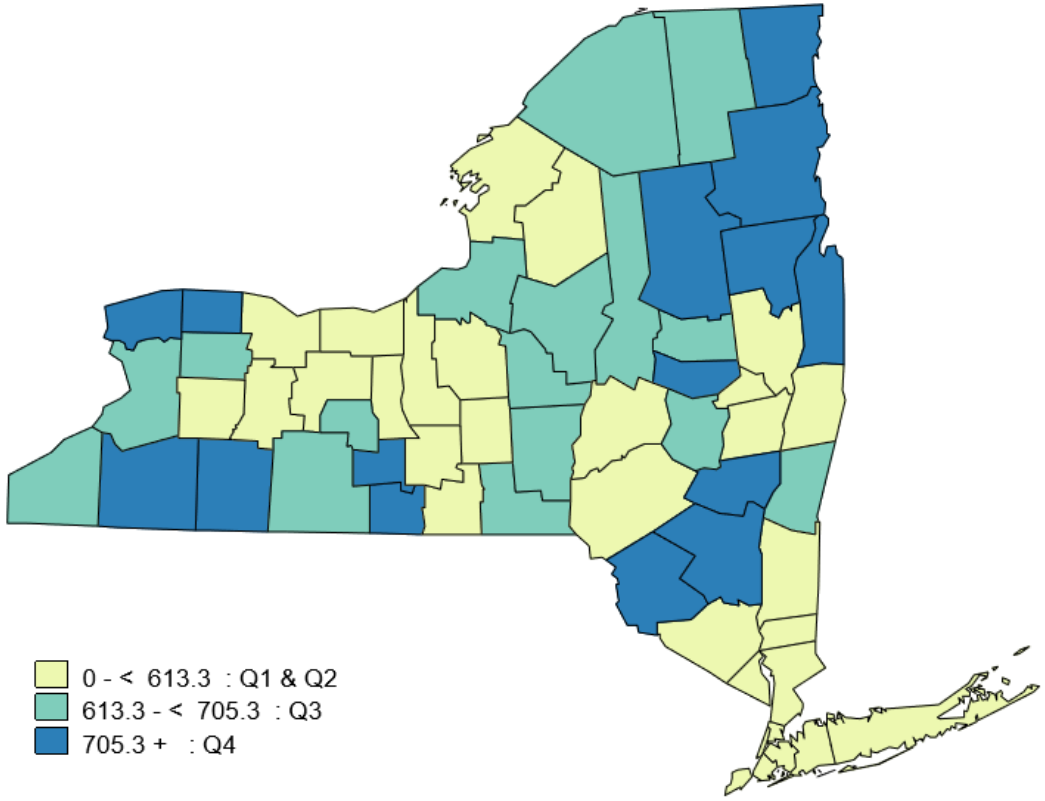
- In 2017, 47,600 Americans died of an opioid overdose
- Death rate from all opioids (including heroin) now exceeds death rate from motor vehicle accidents



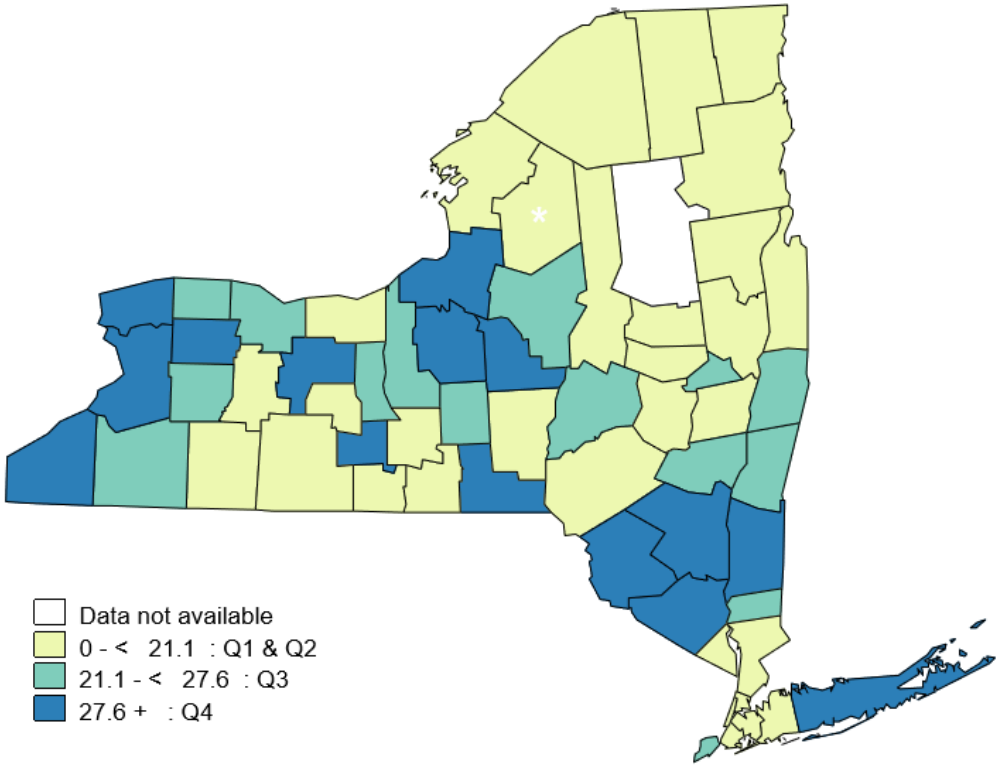
Source: https://www.cdc.gov/drugoverdose/data/analysis.html

Impact on New York State

OPIOID ANALGESIC PRESCRIPTION, CRUDE RATE PER 1,000 POPULATION



OUTPATIENT ED VISIT INVOLVING ANY OPIOID OVERDOSE (RATE PER 100,000 POPULATION



NYS Department of Health. Opioid-related Data in NYS. https://www.health.ny.gov/statistics/opioid/

Opioid Crisis

Before ordering an opioid did you:

- Perform a risk assessment
- Check the PDMP
- Counsel on the medication risks
- Make sure it was not for back pain or headaches

Change habits, remove preselected opioids from order sets, fight the impulse to prescribe opioids!

Alternative to Opioid Principles

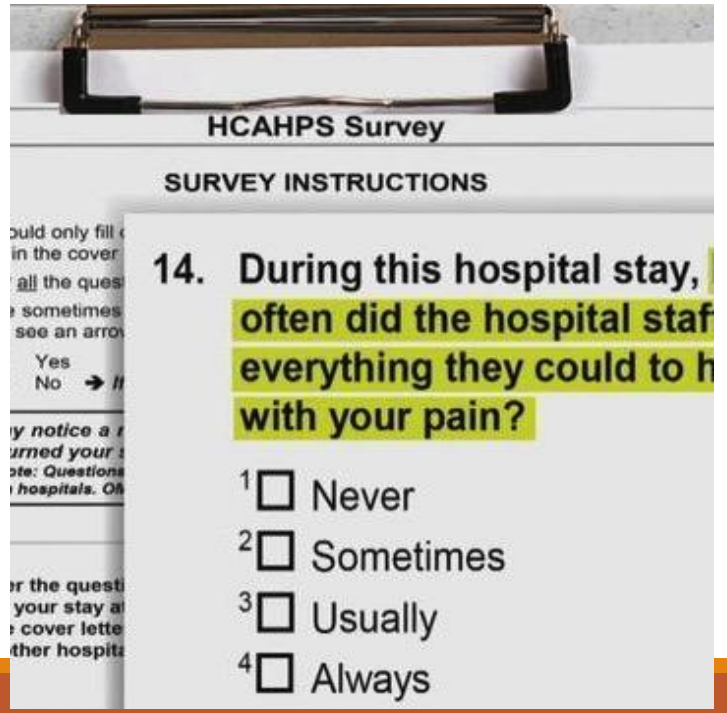
- Non-opioid first!
- Opioids as rescue therapy and not used liberally
- Multimodal and holistic pain management
- Optimize use of pathways (kidney stones, back pain, fractures, headache, chronic abdominal pain)
- More Patient engagement: realistic goals, respect dangers and side effects of opioids

Patient Satisfaction and Opioids

Stader		Press Ganey (%ile) Benchmarks						
116	Satisfaction Element	50th	75th	90th	2Q16	3Q16	4Q16	1Q17
	Overall Communication with Doctors	68.0	73.2	78.5	80.0	89.6	79.1	100.0
	Courtesy	71.6	76.7	81.6	70.6	100.0	87.0	100.0
	Listen Carefully	68.4	73.5	78.8	81.3	84.2	81.0	100.0
	Explained Treatments	65.9	71.4	77.0	81.3	84.2	71.4	100.0
	Attentive to Comfort	66.1	71.7	77.3	87.5	89.5	76.2	100.0
	Pain Management	55.3	61.8	68.8	73.3	81.3	70.0	86.7
	Total N				17	20	22	20

1. Pain? Do you want anything for it?
2. Perform a risk assessment. Driving?
3. Offer alternatives first. Opioids last.
4. Establish norms. No opioids for back pain, headache.
5. Discuss harms, risks, why you aren't RX'ing opioids. Addiction, constipation, balance/cognition issues.
6. Blame 3rd parties. Preserve the fact you are on patient's side.

BIGGEST KEY: BE NICE, SHOW YOU CARE ABOUT THEM.



Question

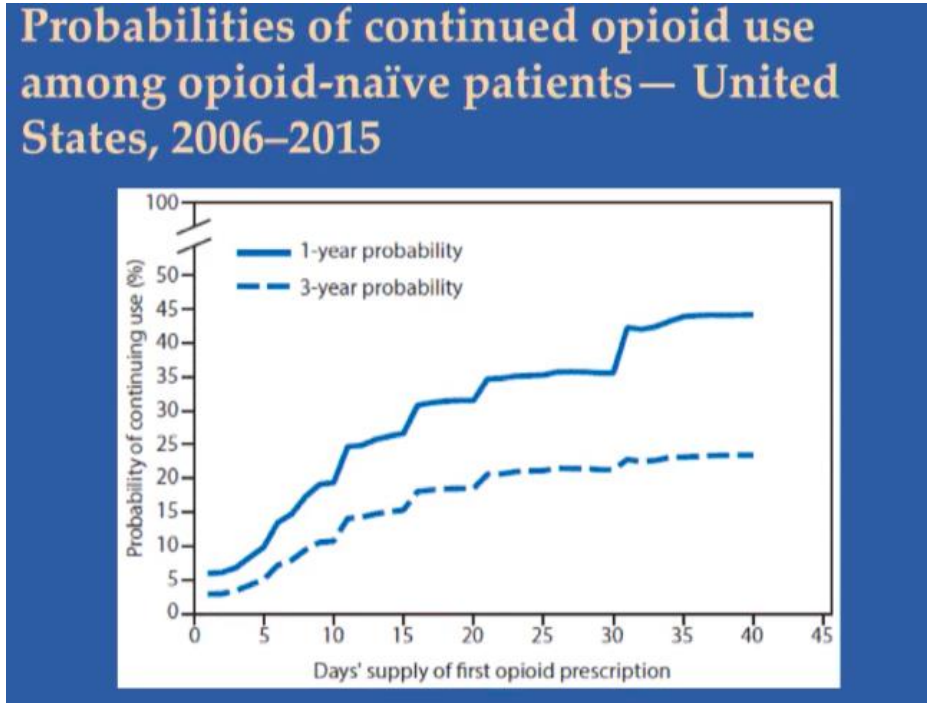
At one year, what percentage of opioid naive patients who receive a prescription for a 30 day supply are still on opioids?

a. 5 %

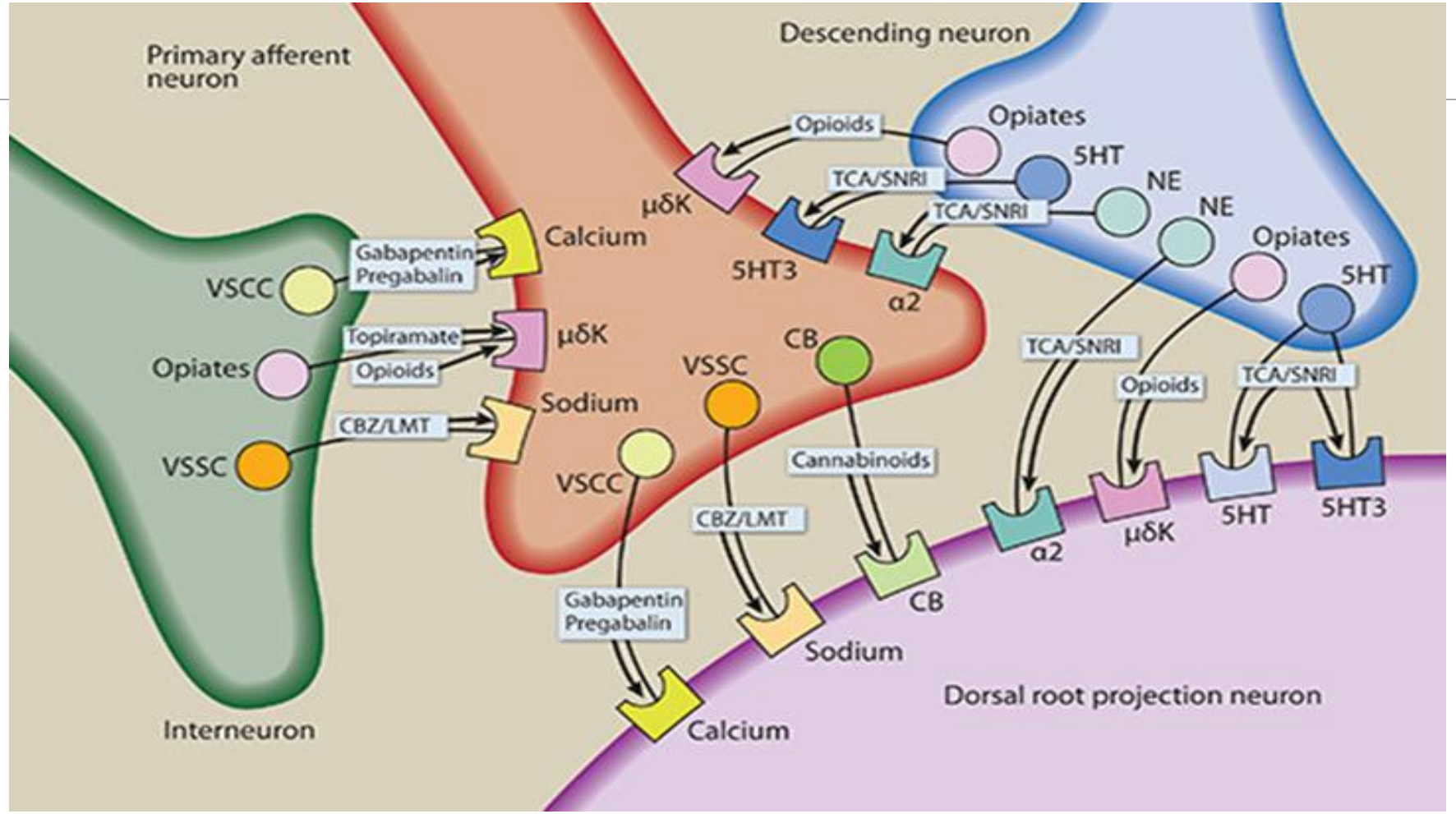
b. 20%

c. 35%

d. 50%



CERTA approach – Multimodal



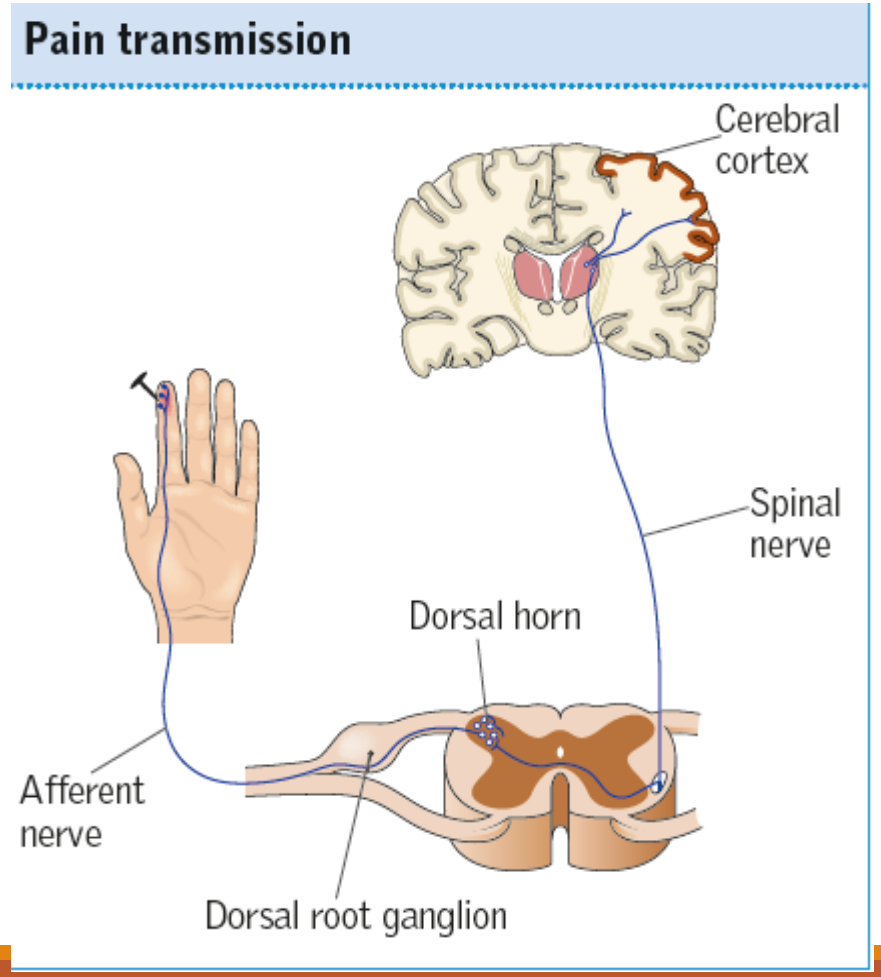
Source: http://www.propofology.com/infographs/certa-concept-of-analgesia

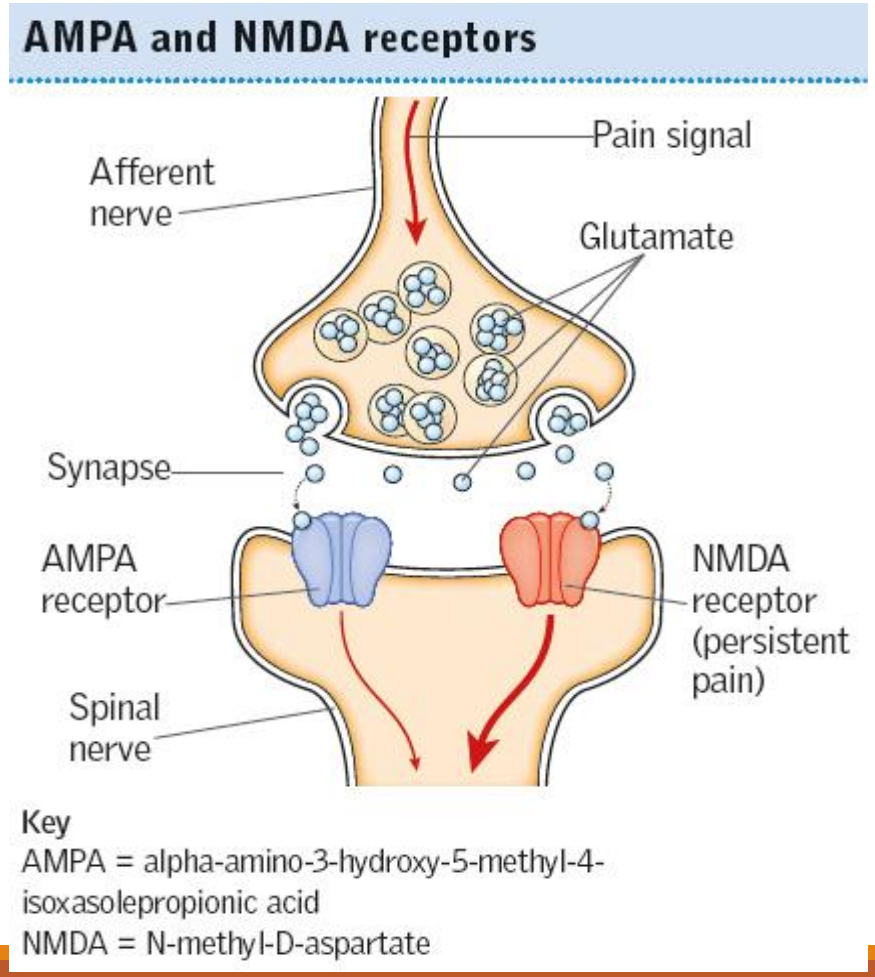
Examples

- **C**hannels:
  - Sodium (Lidocaine)
  - Calcium (Gabapentin)
- **E**nzymes:
  - COX 1,2,3 (NSAIDS)
- **R**eceptors:
  - MOP/DOP/KOP (Opioids)
  - NMDA (Ketamine/Magnesium)
  - GABA(Gabapentin/Sodium Valproate)
  - 5HT1-4(Haloperidol/Ondansetron/Metoclopramide)
  - D1-2(Haloperidol/Chlorpromazine/Prochlorperazine)

Evidence for use of non-opioid alternatives

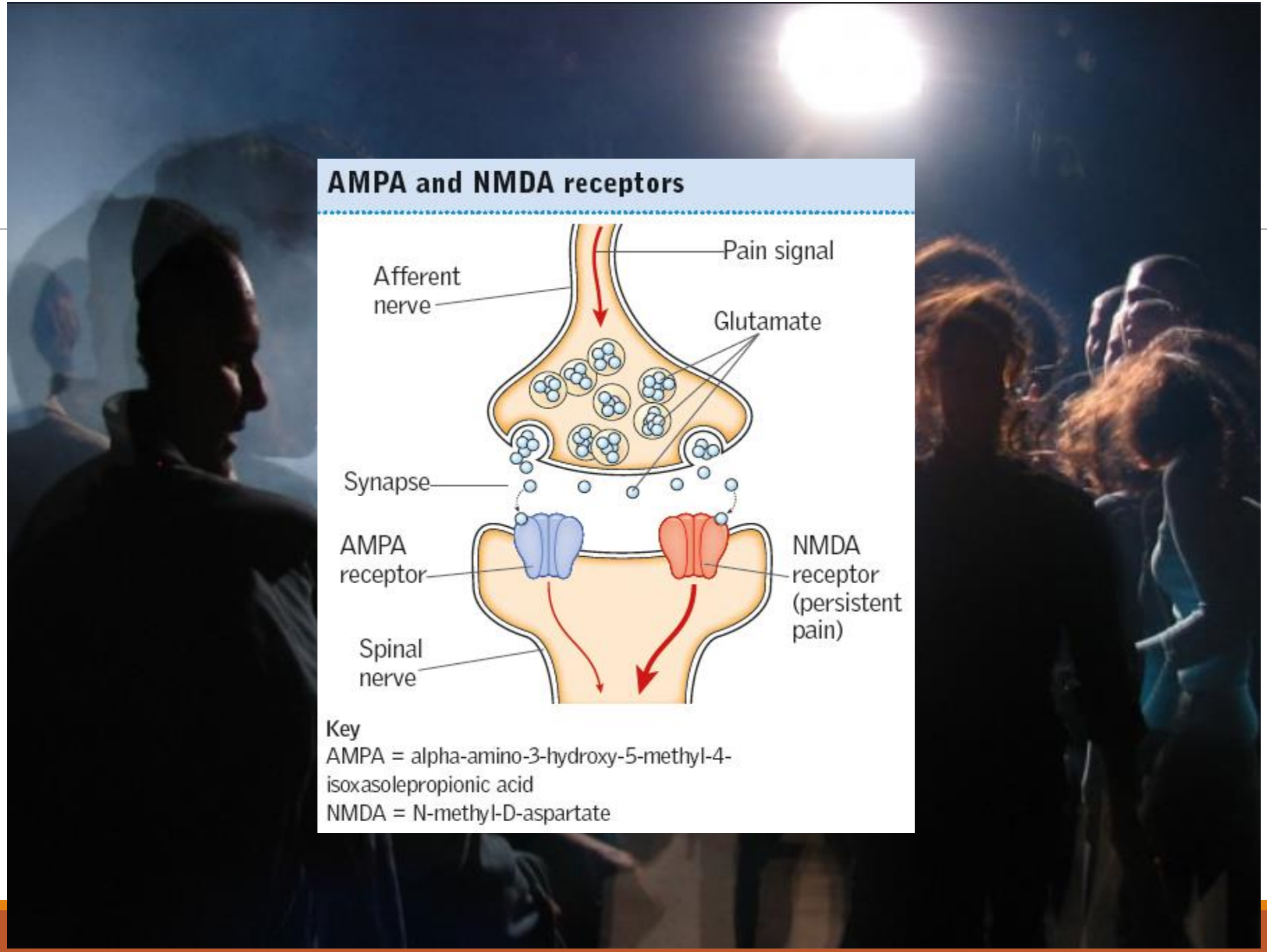
Pain transmission via NMDA receptor[1]





Ketamine[1-4]

- **Therapeutic category**
  - N-methyl D-Aspartate (NMDA) receptor antagonist
  - Variety of effects
    - Respiratory system
      - Bronchodilation
    - Cardiovascular system
      - Increase in cardiac output, blood pressure, heart rate
    - Central nervous system
      - Analgesia
      - Anesthesia
      - Emergence phenomenon
      - Dissociation


AMPA and NMDA receptors
Pain signal
Afferent nerve
Glutamate
Synapse
AMPA receptor
NMDA receptor (persistent pain)
Spinal nerve
Key
AMPA = alpha-amino-3-hydroxy-5-methyl-4-isoxasolepropionic acid
NMDA = N-methyl-D-aspartate

Pharmacokinetics[2]

Onset/Duration	Distribution	Metabolism	Elimination
Onset: IV: within 30 seconds IM: within 10-15 mins Duration: IV (anesthesia): 5-10mins	Vd= 2.4L/kg $T_{1/2}$ = Alpha: 10-15 minutes; Beta: 2.5 hours 27% protein bound	Hepatic	91% urine

Academic Emergency Medicine

The Journal of Emergency Medicine, Vol. 52, No. 5, pp. 601–608, 2017

0736-4679/$ - see front matter

ORIGINAL CONTRIBUTION

CME

Low-dose Ketamine Improves Pain Relief in Patients Receiving Intravenous Opioids for Acute Pain in the Emergency Department

0.3mg/kg/dose IV

Francesca L. Beaudoin, MD, MS, Charlie Lin, Wentao Guan, MS, and Roland C. Merchant, MD, MPH, ScD

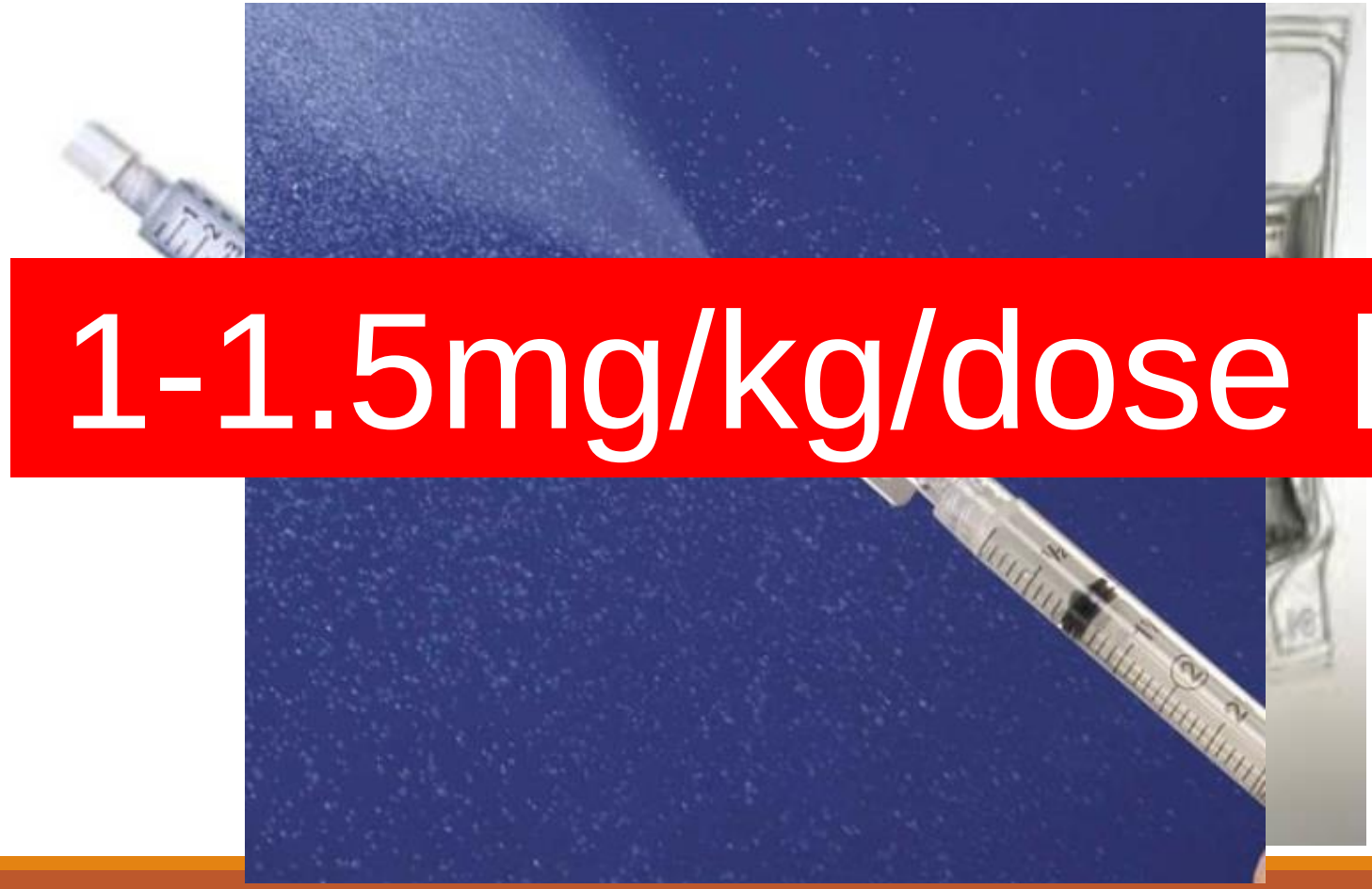
Abstract

Objectives: Low-dose ketamine has been used perioperatively for pain control and may be a useful adjunct to intravenous (IV) opioids in the control of acute pain in the emergency department (ED). The aim of this study was to determine the effectiveness of low-dose ketamine as an adjunct to morphine versus standard care with morphine alone for the treatment of acute moderate to severe pain among ED patients.

The objective of our study was to evaluate ketamine in subdissociative doses as an adjunct for acute pain in the ED.

☐ **Keywords—acute pain; analgesia; subdissociative dose; ketamine**

Administration[1-4]



Administration[7]

TABLE 6. Summary of ASRA/AAPM Recommendations for Subanesthetic Ketamine i

Recommendation Category	Recommendation
Indications for use	(1) Perioperative use in surgery with moderate to severe postoperative pain (2) Perioperative use in patients with opioid tolerance (3) As analgesic adjunct in opioid-tolerant patients with sickle cell crisis (4) As analgesic adjunct in patients with OSA
Dosing range	Bolus: up to 0.35 mg/kg Infusion: up to 1 mg/kg per hour
Relative contraindications	(1) Poorly controlled cardiovascular disease (2) Pregnancy, psychosis (3) Severe hepatic disease, ie, cirrhosis (avoid), moderate hepatic disease (caution) (4) Elevated intracranial pressure, elevated intraocular pressure
Personnel	Supervising clinician: a physician experienced with ketamine (anesthesiologist, critical care physician, pain physician, emergency medicine physician) who is ACLS certified and trained in administering moderate sedation Administering clinician: registered nurse or physician assistant who has completed formal training in safe administration of moderate sedation and is ACLS certified

OPEN

Cor
Infu
S
An

mine
rican
the
ican

Eric S. Sc
Ajay D.

MD, PhD,‡
vis, MD,††

Backgroun
acute pain, b
of treatment
individuals

nmittee then re-
ittee chair were
preliminary con-
ner revisions via

Which would you choose?

AG is a 45 year old male who presents to the ED with acute abdominal pain. The physician would like to initiate ketamine and inquires with you, the pharmacist, on whether ketamine should be administered as a push versus slow infusion over 10-15 minutes. Your answer is….

A. Push

B. Infuse over 10-15 minutes

C. It does not matter

Clinical consideration: IVP or IVPB?

Am J Emerg Med. 2017 Aug;35(8):1095-1100. doi: 10.1016/j.ajem.2017.03.004. Epub 2017 Mar 3.

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.

Motov S[1], Mai M[2], Pushkar I[2], Likourezos A[2], Drapkin J[2], Yasavolian M[2], Brady J[3], Homel P[4], Fromm C[2].

Author information

Abstract

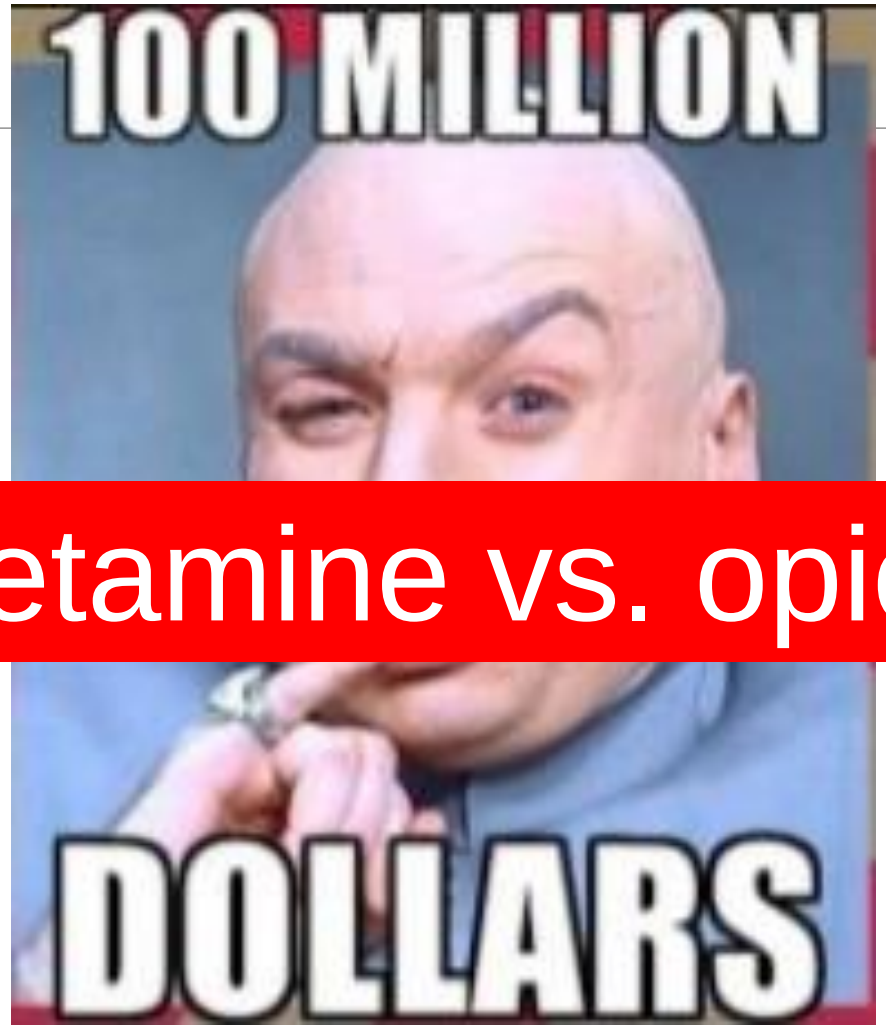
STUDY OBJECTIVE: Compare adverse effects and analgesic efficacy of low-dose ketamine for acute pain in the ED administered either by single intravenous push (IVP) or short infusion (SI).

METHODS: Patients 18-65, presenting to ED with acute abdominal, flank, or musculoskeletal pain with initial pain score≥5, were randomized to ketamine 0.3mg/kg by either IVP or SI with placebo double-dummy. Adverse effects were evaluated by Side Effects Rating Scale for Dissociative Anesthetics (SERSDA) and Richmond Agitation-Sedation Scale (RASS) at 5, 15, 30, 60, 90, and 120min post-administration; analgesic efficacy was evaluated by Numerical Rating Scale (NRS).

RESULTS: 48 patients enrolled in the study. IVP group had higher overall rates of feeling of unreality on SERSDA scale: 92% versus 54% (difference 37.5%; p=0.008; 95% CI 9.3-59.5%). At 5min median severity of feeling of unreality was 3.0 for IVP versus 0.0 for SI (p=0.001). IVP also showed greater rates of sedation on RASS scale at 5min: median RASS -2.0 versus 0.0 (p=0.01). Decrease in mean pain scores from baseline to 15min was similar across groups: 5.2±3.53 (95% CI 3.7-6.7) for IVP; 5.75±3.48 (95% CI 4.3-7.2) for SI. There were no statistically significant differences with respect to changes in vital signs and need for rescue medication.

CONCLUSION: Low-dose ketamine given as a short infusion is associated with significantly lower rates of feeling of unreality and sedation with no difference in analgesic efficacy in comparison to intravenous push.

KEYWORDS: Analgesia; Emergency department; Infusion; Ketamine



Ketamine vs. opioids

77 Emergency (2014); 2 (2): 77-80

OPEN ACCESS

ORIGINAL RESEARCH

Comparison of Intravenous Ketamine with Morphine in Pa
Bones Fractures: a Double Blind Randomized Clini

Saeed Majidinejad, Mehrdad Esmailian, Mehrdad Emadi*

Department of Emergency Medicine, Isfahan University of Medical Sciences, Isf

Abstract

Introduction: The selective medication for pain control in many clinical situations is m
tions prevent its widespread use. Ketamine has been introduced as an alternative for n

Accepted Manuscript

Intravenous subdissociative-dose ketamine versus morphine for acute geriatric pain in the Emergency Department: A randomized controlled trial

Sergey Motov, Stefan Mann, Jefferson Drapkin, Antonios Likourezos, Elizabeth Yetter, Jason Brac Christian Fromm, John Marshall

Intravenous Subdissociative-Dose Ketamine Versus Morphine for Analgesia in the Emergency Department: A Randomized

MPH;
n, MD

Randomized Controlled Feasibility Trial of Intranasal Ketamine Compared to Intranasal Fentanyl for Analgesia in Children with Suspected Extremity Fractures

Stacy L. Reynolds, MD, Kathleen K. Bryant, MD, Jonathan R. Studnek, PhD, Melanie Hogg, Connell Dunn, Megan A. Templin, MS, Charity G. Moore, PhD, MSPH, James R. Young, MD, Katherine Rivera Walker, BSN, and Michael S. Runyon, MD, MPH

A related article appears on page 1511.

ABSTRACT

Objectives: We compared the tolerability and efficacy of intranasal subdissociative ketamine to intranasal fentanyl for analgesia of children with acute traumatic pain and investigated the feasibility of a larger noninferiority trial that could investigate the potential opioid-sparing effects of intranasal ketamine.

Compariso
in patients with renal colic☆

Mohammad Reza Farnia, MD [a], Alireza Jalali, MD [b], Elnaz Vahidi, MD [c], Mehdi Momeni, MD [c], Javad Seyedhosseini, MD [c], Morteza Saeedi, MD [c,*]

[a] *Kermanshah University of Medical Sciences, Imam Reza Hospital, Emergency Medicine Department, Kermanshah, Iran*
[b] *Tehran University of Medical Sciences, Shariati Hospital, Emergency Medicine Department, Tehran, Iran*
[c] *Emergency Medicine Research Center, Emergency Medicine Department, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran*

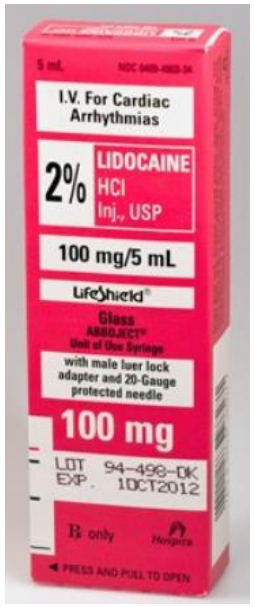
First author year, country	Sample size	Age range	Chief complaint	Intervention	Comparison	Measured outcome	Result	Conclusion
Majidinejad 2014, Iran [7]	n=126	18-55 years	Fractures of long bones	IV ketamine 0.5 mg/kg (n=63)	IV morphine 0.1 mg/kg (n=63)	**Primary:** Mean severity of pain before admin of medications and 10 minutes after	Before administration: ketamine 8.9±0.8 vs. morphine: 8.8±0.8 (p=0.32) After administration: ketamine 2.7 ± 1.8 vs. IV morphine: 2.4±1.5 (p=0.28)	No significant difference (p>0.05)
Motov 2015, United States [8]	n=90	18-55 years	acute abdominal, flank, back, or musculoskeletal pain and pain score of 5 or more on a 11-point NRS	IV ketamine 0.3 mg/kg in 10 ml of NS (n=45)	IV morphine 0.1 mg/kg in 10 ml of NS (n=45)	**Primary:** Mean NRS pain scores at 30 minutes.	ketamine: 4.1 ± 3.2 vs morphine: 3.9 ± 3.1 (mean difference: 0.2 [95% CI: -1.19 to 1.46])	No significant difference (p>0.05)
Motov 2018, United States [9]	n=60	≥65 years	acute abdominal, flank, back, or musculoskeletal pain and pain score of 5 or more on a 11-point NRS	IV ketamine 0.3 mg/kg in 100 ml of NS (n=30)	IV morphine 0.1 mg/kg in 100 ml of NS (n=30)	**Primary:** Mean NRS pain scores at 30 minutes.	ketamine: 4.2±3.4 vs morphine: 4.4±3.1 (mean difference: -0.2 [95% CI: -1.93 to 1.46])	No significant difference (p>0.05)
Reynolds 2017, United States [10]	n=87	4-17 years	suspected single-extremity fracture requiring analgesia with an initial pain score ≥ 4 (4-10 years) or an Adult pain score of at least 3 (11-17 years)	IN ketamine 1mg/kg (n=43)	IN fentanyl 1.5 µg/kg (n=44)	**Primary:** Mean pain scale score reduction in FPS-R at 30 mins after admin, mean± SD (mean difference [95% CI])	IN ketamine: 46±34 vs. IN fentanyl: 39±29 (7[-7 to 21])	No significant difference (p>0.05)

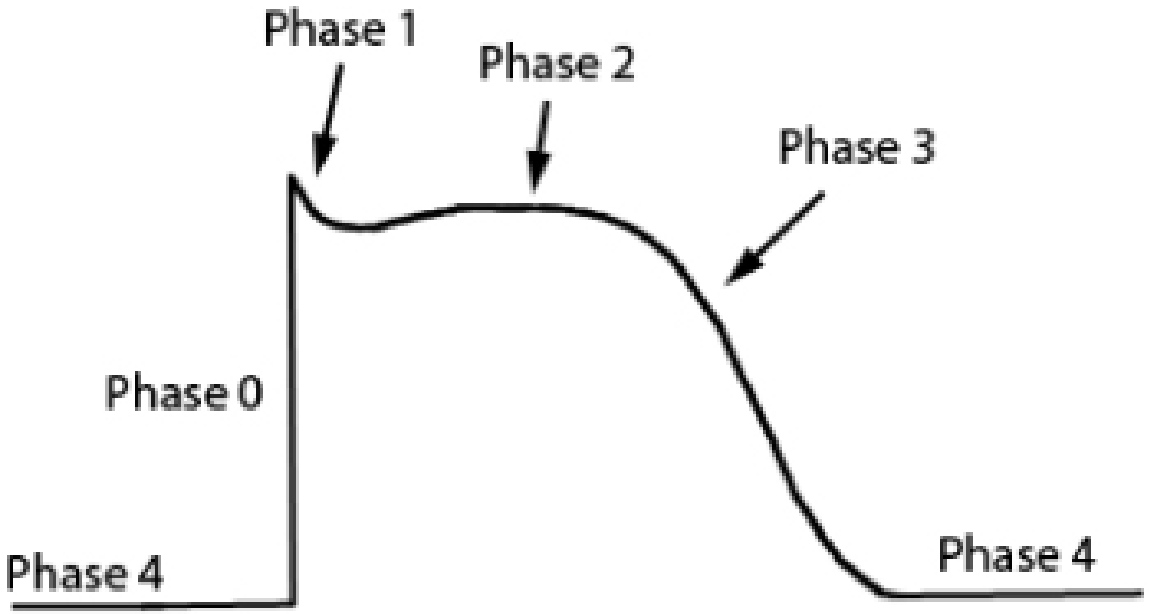
Clinical considerations

- Route
  - IV access?
  - Nausea/vomiting?
  - Readily available in the ED?
  - Procurement turnaround?
- Safety (Avoid in…)
  - Hemodynamic instability (high blood pressure)
  - Baseline psychiatric condition
  - Altered mental status

Lidocaine[11]

- **Therapeutic category**
  - Class Ib amide antiarrhythmic
- **Mechanism of action**
  - Blocks sodium channel ⟹ Decrease conduction velocity
- **Adverse event profile**
  - Headache, dizziness, flushing, edema
  - Twitching, seizure, arrhythmia
- **Availability**
  - 100mg pre-filled syringe
  - 1%, 2% injection vial





Phases	Channels involved	Action
0 (Rapid depolarization)	Sodium	Sodium influx, Rapid depolarization of atrial and ventricular tissue
1 (Initial repolarization)	Potassium	Potassium efflux. Calcium starts to move into intracellular space which causes a slower depolarization.
2 (Plateau phase)	Calcium	Calcium influx into intracellular space continues
3 (Repolarization)	Potassium	Active potassium efflux results in repolarization
4 (Slow depolarization)	Sodium	Gradual depolarization, abrupt influx of sodium allows rapid depolarization

Pharmacokinetics[11]

Onset/Duration	Distribution	Metabolism	Elimination
Onset: 45-90 seconds Duration: 10-20 minutes	Vd= 0.7-2.7L/kg $T_{1/2}$ = 7-30 minutes 60-80% protein bound	Hepatic	Urine

TOXICOLOGY/SYSTEMATIC REVIEW/META-ANALYSIS

Safety and Efficacy of Intravenous Lidocaine for Pain Management in the Emergency Department: A Systematic Review

Lucas Oliveira L e Silva; Kristin Scherber, PharmD; Daniel Cabrera, MD; Sergey Motov, MD; Patricia L Erwin, MLS;

1-1.5mg/kg IV

Study objective: We evaluate the safety and efficacy of intravenous lidocaine in adult patients with acute and chronic pain who are undergoing pain management in the emergency department (ED).

oid naïve. On physical examination, there was no midline tenderness along the spine, but moderate left-sided cervical paraspinal tenderness to palpation was noted. There was diffuse tenderness to palpation of the left arm, most profound at the distal third of the left clavicle. Range of motion was limited

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

lication included alb-
s needed. Also, 7 days
gnosed with a 3-mm
. He was prescribed
every 4 to 6 hours for pain and tamsulosin 0.4 mg once daily for passing of the stone. On each day during the 7-day period, JA consumed 12 tablets of oxycodone/acetaminophen and 1 capsule of tamsulosin. No adjunctive analgesics or nonpharmacological therapies were used. Over the past 2 days, he had experienced increasing episodes of pain, nausea, and vomiting. JA had also noted small traces of blood in his vomit, raising suspicion for a gastrointestinal injury. On physical exami-

Billy Sin, PharmD, BCPS
LIU Pharmacy (Arnold and Marie Schwartz College of Pharmacy), New York, NY, USA
The Brooklyn Hospital Center, New York, NY, USA
Muhammad Effendi, PharmD Candidate
LIU Pharmacy (Arnold and Marie Schwartz College of Pharmacy), New York, NY, USA
Christopher Bjork, MD
Sheena Punnapuza, MD
The Brooklyn Hospital Center, Brooklyn, NY, USA

References

Lidocaine vs. opioids

Emergency. 2017; 5 (1): e82
http://dx.doi.org/10.22037/emergency.v5i1.18894

OPEN ACCESS

ORIGINAL RESEARCH

Intravenous Lidocaine Compared to Fentanyl in Renal Colic Pain Management; a Randomized Clinical Trial

Hassan Motamed[1], **Mohammadreza Maleki Verki**[1]*

1. Emergency Medicine Department, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

Received: September 2017

Abstract: **Introduction:** Using alpha blockers such as intravenous (IV)
acute pain. Therefore, the current study was designed with
in comparison to IV fentanyl in pain management of patien

RESEARCH ARTICLE Open Access

Effectiveness of intravenous lidocaine versus intravenous morphine for patients with renal colic in the emergency department

Hassan Soleimanpour[1*], Kamaleddin Hassanzadeh[2], Hassan Vaezi[1], Samad EJ Golzari[3,4], Robab Mehdizadeh Esfanjani[5] and Maryam Soleimanpour[6]

Abstract

Background: Despite the fact that numerous medications have been introduced to treat renal colic, none has been proven to relieve the pain rapidly and thoroughly. In this study, we aimed at comparing the effects of intravenous lidocaine versus intravenous morphine in patients suffering from renal colic.

Methods: In a prospective randomized double-blind clinical trial performed in the emergency department of Imam

First author year, country	Sample size	Age range	Chief complaint	Intervention	Comparison	Measured outcome	Result	Conclusion
Motamed 2017, Iran [12]	n=90	18-65 years	Renal colic	IV lidocaine 1.5 mg/kg (n=45)	IV fentanyl 1.5 µg/kg (n=45)	**Primary:** 100 mm VAS score at designated time intervals following AOI	At 30 min: **Mild pain** lidocaine: 22 (48.9%) vs. fentanyl: 25 (55.6%) **Moderate pain** lidocaine: 10 (22.2%%) vs. fentanyl: 7 (15.6%) **Severe pain** lidocaine: 13 (28.9%) vs. fentanyl: 13 (28.9%)	No significant difference ($p>0.05$)
Soleimanpour 2012, Iran [13]	n=240	18-65 years	Pain radiating to genitalia and groin, and tenderness in costovertebral angle	IV lidocaine solution 1.5 mg/kg (n=120)	IV morphine 0.1 mg/kg (n=120)	**Primary:** 11 point mean NRS score at 5 min AOI	IV lidocaine: 3.18 ± 2.2 vs. IV morphine: 4.45 ± 2.1	Patient who received IV lidocaine had more pain relief

Clinical considerations

- Product to use
  - Need to be preservative free
- Data describes use of IV
  - No mention of IVP or IVPB (IVPB preferred)
  - Infuse with fluids to avoid potential adverse events
  - Cardiac monitor recommended
- Safety (Avoid in…)
  - Hemodynamic instability (electrolyte imbalance)
  - History of arrhythmia
  - Liver dysfunction

Test your knowledge

AG is a 42 (60kg) year old female who presents to the ED with severe left leg fracture after slipping on the sidewalk. Initial vital signs include: HR: 102, BP: 100/72, RR: 12, O_2 sat: 98% on room air. She has a past medical history of asthma and hyperlipidemia. Her reported pain score is 10/10. The patient states that she does not want opioids because "she does not want to be an addict". The physician would like to initiate lidocaine. Which of the following statements would be appropriate plans of treatment for AG?

A. Initiate at dose of 90mg IVPB over 5-10 minutes

B. Ensure patient is on cardiac monitor during therapy

C. Monitor AG for arrhythmia, flushing, headache

D. All of the above

Acetaminophen (IV)

- **Therapeutic category**
  - Non-opioid analgesic
- **Mechanism of action**
  - Activation of descending serotonergic inhibitory pathways in CNS
- **Adverse event profile**
  - Nausea (34%), vomiting (15%)
  - Rash (1-10%)
- **Availability**
  - 1g vial ($48/vial)

Pharmacokinetics[14,15]

Onset/Duration	Distribution	Metabolism	Elimination
Onset: 5-10 minutes Duration: 4-6 hours	Vd= 0.7-1L/kg (high) $T_{1/2}$ = 2-3 hours 60-80% protein bound	Hepatic, mainly via CYP2E1	Renal (<5% unchanged)

What to do when….

Anesthesiology 2005; 102:822–31

Efficacy and Safety of Single and Repeated Administration of 1 Gram Intravenous Acetaminophen Injection (Paracetamol) for Pain Management after Major Orthopedic Surgery

Raymond S. Sinatra, M.D., Ph.D., Jonathan S. Jahr, M.D.,† Lowell W. Reynolds, M.D.,‡ Eugene R. Viscusi, M.D.,§ Scott B. Groudine, M.D.,‖ Catherine Payen-Champenois, M.D.#*

Background: **Intravenous acetaminophen injection (paracetamol) is marketed in Europe for the management of acute**

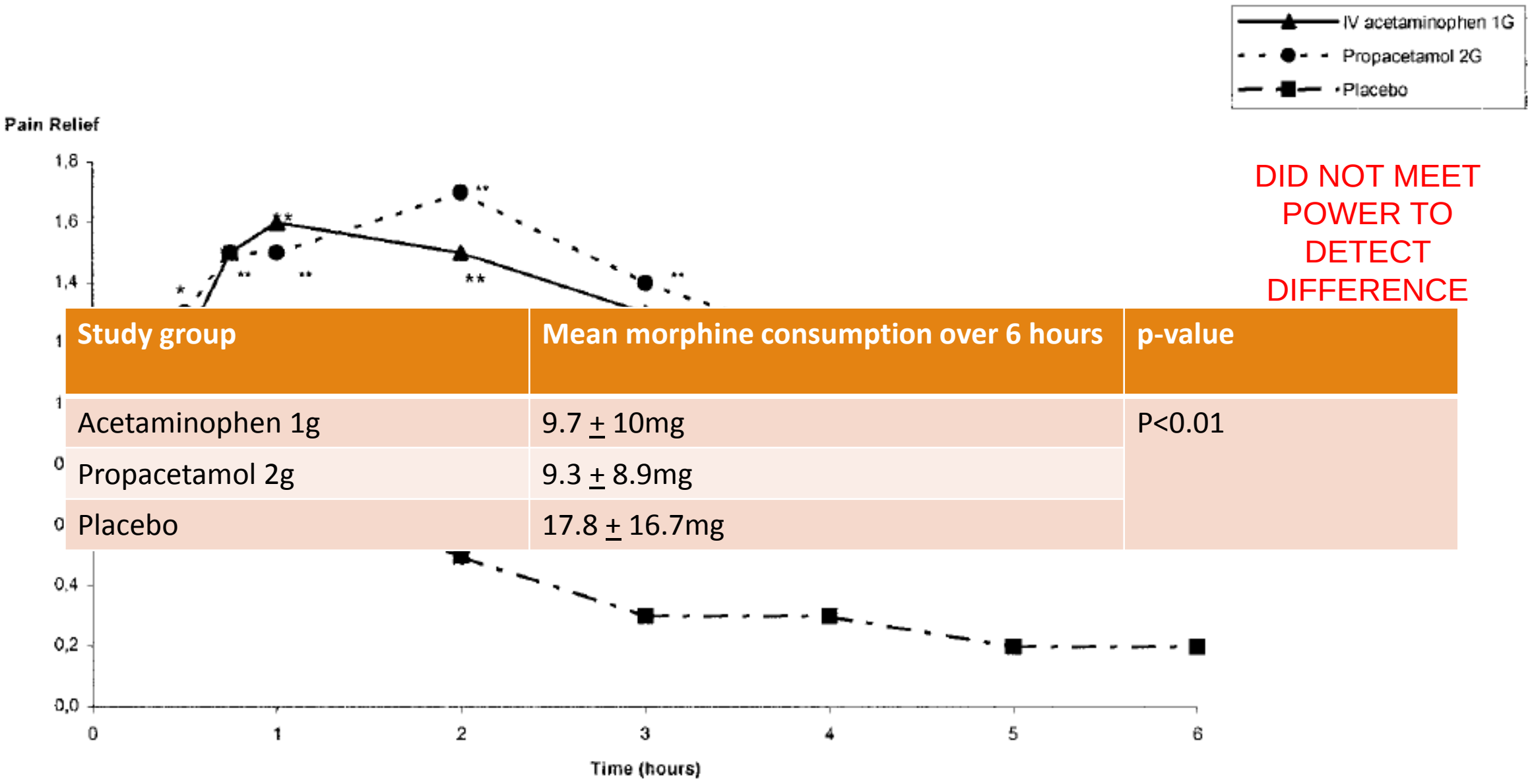
patients treated with intravenous acetaminophen, propacetamol, and placebo, respectively.

Intravenous Paracetamol or Morphine for the Treatment of Renal Colic: A Randomized, Placebo-Controlled Trial

Firat Bektas, MD
Cenker Eken, MD
Ozgur Karadenız, MD
Erkan Goksu, MD
Metin Cubuk, MD
Yildiray Cete, MD

From the Department of Emergency Medicine (Bektas, Eken, Karadeniz, Goksu, Cete) and Department of Radiology (Cubuk), Akdeniz University Faculty of Medicine, Antalya, Turkey.

Study objective: This randomized, placebo-controlled trial evaluates the analgesic efficacy and safety of intravenous single-dose paracetamol and morphine for the treatment of renal colic.



DID NOT MEET POWER TO DETECT DIFFERENCE

Study group	Mean morphine consumption over 6 hours	p-value
Acetaminophen 1g	9.7 ± 10mg	P<0.01
Propacetamol 2g	9.3 ± 8.9mg	
Placebo	17.8 ± 16.7mg	

Academic Emergency Medicine
Official Journal of the Society for Academic Emergency Medicine

American Journal of Therapeutics 0, 1–8 (2016)

PAIN MANAGEMENT/ORIGINAL RESEARCH

Intravenous Paracetamol or Morphine for the Treatment of Renal Colic: A Randomized, Placebo-Controlled Trial

Firat Bektas, MD
Cenker Eken, MD
Ozgur Karadeniz, MD
Erkan Goksu, MD
Metin Cubuk, MD
Yildiray Cete, MD

From the Department of Emergency Medicine (Bektas, Eken, Karadeniz, Goksu, Cete) and Department of Radiology (Cubuk), Akdeniz University Faculty of Medicine, Antalya, Turkey.

Study objective: This randomized, placebo-controlled trial evaluates the analgesic efficacy and safety of intravenous single-dose paracetamol and morphine for the treatment of renal colic.

First author year, country	Sample size	Age	Chief complaint	Intervention	Comparison	Measured outcome	Result	Conclusion
Bektas 2009, Turkey [17]	n=146	18-55 years	Renal colic and "mild" or greater pain intensity on a 4-point verbal rating scale or at least 20 mm on a 100-mm VAS	IV APAP 1 g in 100 mL NS (n=46)	IV morphine 0.1 mg/kg in 100 mL NS (n=51) IV 100 mL NS (n=49)	**Primary:** Median (IQR) change in VAS pain intensity score at 30 minutes	At 30 min **IV morphine: 43 mm** (7-73 mm) **IV APAP: 41.5 mm** (24-63 mm) **Placebo: 24mm** (5-45 mm)	NS (p>0.05)
Masoumi 2014, Iran [18]	n=110	18-55 years	Renal colic	APAP 1g IV over 5-10 mins [n=54]	Morphine 0.1mg/kg IV over 5-10 mins [n=54]	**Primary:** 10-point VAS reduction at 30 min after meds (Mean ± SD)	APAP: 4.7±2.3 vs. morphine 2.9±2.2, (p<0.05)	Significant reduction, favoring APAP
Azizkhani et al., 2013[21]	n=124	≥18 years	Renal colic	APAP 15mg/kg IV over 15 min [n=62]	Morphine 0.1mg/kg IV over 15 min [n=62]	**Primary:** 10-point VAS reduction at 30 min after meds (Mean ± SD)	APAP: 2.4±3.3† vs. morphine: 0.75±1.31†, (p<0.05)	Significant reduction, favoring morphine
Shams Vahdati 2014, [20]	n=60	18-55 years	Headache ≥ 40/100mm on VAS	APAP 1g IV over 10 mins [n=30]	Morphine 0.1mg/kg IV over 10 mins [n=30]	**Primary:** 100mm VAS at 15 min and 30 min after medication administration (Mean ± SD)	15 min: APAP: 33.8mm±22.5 (95%CI: 26-41) vs. morphine: 39.4mm±27.2 (95%CI: 30-49) 30 min: APAP: 63.7mm±21.7 (95%CI: 57-71) vs. morphine: 56.6mm±24.4 (95%CI: 48-65)	NS (p>0.05)

Clinical considerations

- Cost vs. benefit decision
- Already took something with Tylenol?
- Rate of infusion- over 15 minutes
- Safety (Avoid in…)
  - Hypersensitive
  - Liver dysfunction


1958
2009

Propofol[21]

- Proposed mechanisms
  - Enhance GABA activity at GABA-receptor complex (GABA-A)
  - Blocks NMDA-R ; decrease Ca influx
- Induce hypotension (up to 26%), bradycardia (3%)
  - Have epinephrine / atropine readily available
- Phenol derivative (low aqueous solubility)
  - Drug is in lipid vehicle, 1.1kcal/ml
  - Made from 10% soybean oil

Pharmacokinetics[21]

Onset/Duration	Distribution	Metabolism	Elimination
Onset: 9-50 seconds Duration: 3-10 minutes	Vd= 2-10L/kg (high) $T_{1/2}$ = initial: 40 minutes. terminal: 4-7 hours 97-99% protein bound	Hepatic, mainly via CYP2E1	Renal

PAIN MEDICINE
Volume 3 • Number 4 • 2002

Propofol: A New Treatment Strategy for Refractory Migraine Headache

Jacqueline Drummond-Lewis, MD, and Corey Scher, MD

Anesthesiology Department, Tulane University Health Science Center, New Orleans, Louisiana

ABSTRACT

1mg/kg IV

fering from refractory migraine headaches [1–3]. Case reports over the last few years have appeared in the medical literature describing the use of propofol for migraine treatment. Dosing regimens are not clear, and mechanisms of action to terminate or markedly curtail ongoing intractable headaches are not described.

This case report, of two hospitalized patients with refractory migraine, increases the existing literature on the use of propofol therapy in migraine headache. In the first case, three different scenarios and dosages are described in the same patient. In the second case, the use of different dosages of propofol is described. A self-reported scale was employed by the patients to determine the efficacy of propofol therapy. In the first case, the patient's self-reported migraine score was an average of 100/100 and decreased to 10/100. In the second case, the patient's self-reported migraine score improved from 92/100 to 40/100. We propose that the improvements in the self-reported migraine score in both patients after propofol therapy may be due to $GABA_A$ agonist effects and cerebral vasoconstriction.

Key Words. Propofol; Migraine Headache; $GABA_A$ Receptors; 5-HT Receptors

CASE REPORT Open Access

Improvement of refractory migraine headache by propofol: case series

Hassan Soleimanpour[1*], Aliakbar Taheraghdam[2], Rouzbeh Rajaei Ghafouri[1], Ali Taghizadieh[1], Karim Marjany[3] and Maryam Soleimanpour[4]

Abstract

Background: Several studies have been conducted on managing migraine headaches and developing effective medications for decreasing migraine-associated pain.

Case presentation: Intravenous propofol was prescribed (10 mg every 5 min) for eight patients with intractable migraine headaches visiting the Emergency Department. The average pain score experienced by patients was recorded using the Visual Analogue Scale at the beginning of the treatment procedure and following the injection for 30 min (5-min intervals). The patients' reported pain scores decreased significantly ($P = 0.01$) from 8.87 ± 0.83 (CI: 8.17, 9.57) to 1.12 ± 0.83 (CI: 0.43, 1.82) before and 30 min following the injection.

Discussion: It seems that in the treatment of intractable migraine headaches, GABAergic receptors, compared to the normal conditions, have a lower activity status.

Conclusion: Because of the high tendency of propofol to GABAergic receptors, it probably changes this physiological condition by activating the receptors, which results in a significant pain reduction.

Keywords: Propofol, Migraine headache, Visual analogue scale, Emergency department, GABAergic receptors

Case	Gend	mptoms
1	Male	tophobia
2	Femal	
3	Femal	to/phonophobia
4	Femal	
5	Femal	to/phonophobia
6	Male	
7	Femal	
8	Femal	to/phonophobia

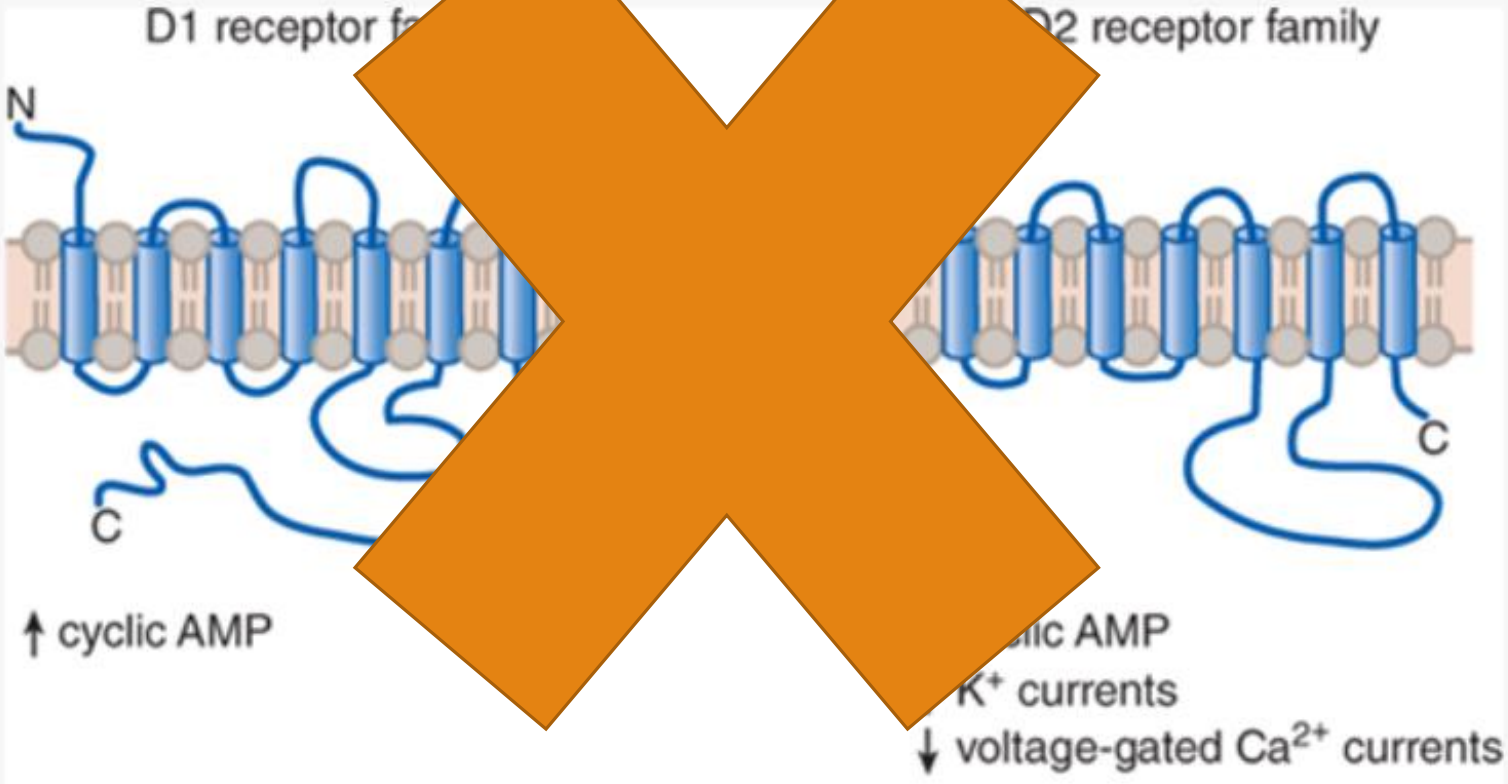
Test your knowledge

AK is a 28 yo female with a history of migraine. Today, she presents to the ED with severe headache, and is sensitive to light and sound. Her vitals signs include: HR: 100, BP: 102/72, RR: 14, O_2 sat: 98% on room air. Two hours prior to visiting the ED, she self-administered APAP 650mg with no relief. In the ED, she has been prescribed ketorolac 30mg IV, dexamethasone 10mg IV, and metoclopramide 10mg IV. Despite these therapies, there has not been any improvements.

Based on available literature, which of the following intravenous agents should be used for AK?

A. Acetaminophen
B. Ketamine
C. Propofol
D. Morphine

The two subfamilies of DA receptors and their major signaling pathways.



Haloperidol[24,25]

- **Therapeutic category**
  - 1st generation antipsychotic
- **Adverse event profile**
  - Extrapyramidal reaction (>10%), hyperkinesia, abdominal pain
- **Availability**
  - 5mg/ml (lactate injection)

The Journal of Emergency Medicine, Vol. ■, No. ■, pp. 1–9, 2015

0736-4679/$ - see front matter

ELSEVIER

http://dx.doi.org/10.1016/j.jemermed.2015.03.023

Pharmacology in Emergency Medicine

A RANDOMIZED CONTROLLED TRIAL OF INTRAVENOUS HALOPERIDOL VS. INTRAVENOUS METOCLOPRAMIDE FOR ACUTE MIGRAINE THERAPY IN THE EMERGENCY DEPARTMENT

Matthew E. Gaffigan, MD,* David I. Bruner, MD,† Courtney Wason, BS,* Amy Pritchard, DO,‡ and Kenneth Frumkin, MD, PHD*

*Naval Medical Center Portsmouth, Portsmouth, Virginia, †Naval Medical Center San Diego, San Diego, California, and ‡Naval Hospital Camp Pendleton, Camp Pendleton, California

Reprint Address: David I. Bruner, MD, Naval Medical Center San Diego, 8022 Paseo del Ocaso, La Jolla, CA 92037

ORIGINAL CONTRIBUTION

CME

Randomized Controlled Double-blind Trial Comparing Haloperidol Combined With Conventional Therapy to Conventional Therapy Alone in Patients With Symptomatic Gastroparesis

Carlos J. Roldan, MD, Kimberly A. Chambers, MD, Linda Paniagua, MD, Sonali Patel, MD, Marylou Cardenas-Turanzas, MD, DrPH, and Yashwant Chathampally, MD

ABSTRACT

Objective: Gastroparesis is a debilitating condition that causes nausea, vomiting, and abdominal pain.

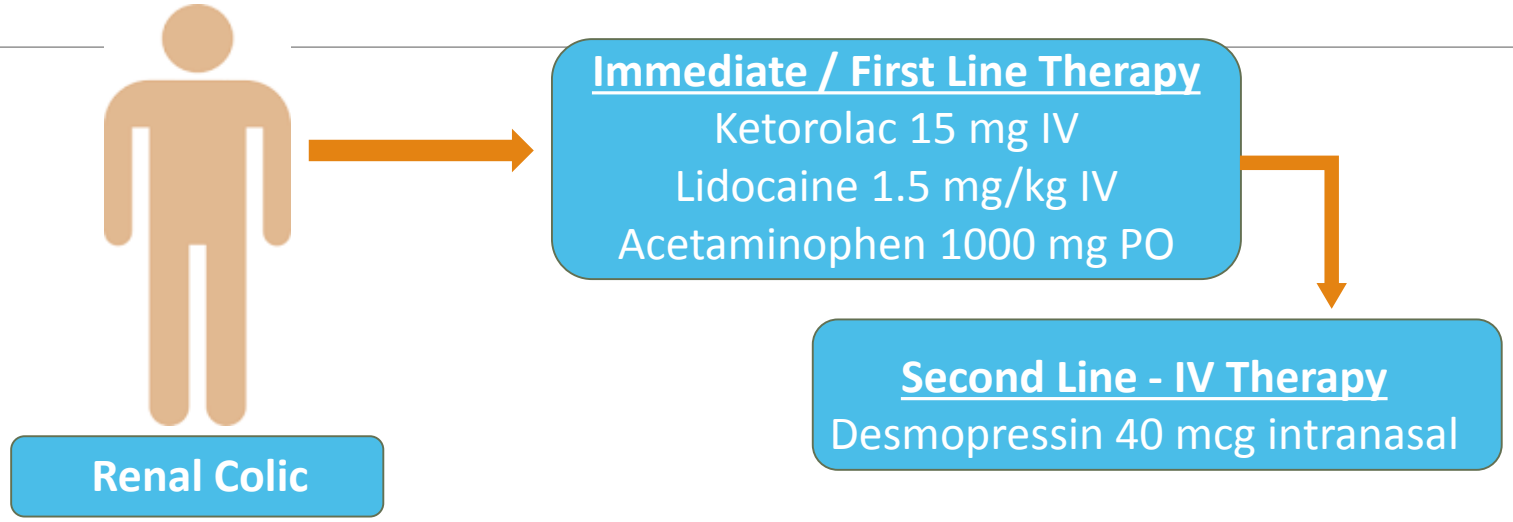
First author year, country	Sample size	Age	Chief complaint	Intervention	Comparison	Measured outcome	Result	Conclusion
Gaffigan 2015, United States [27]	n=146	18-50 years	Migraine with at least (2 of following) 1. Unilateral location 2. Throbbing character 3. Worsening pain with routine activity	IV haloperidol 5mg over 2 mins (n=31)	IV metoclopramide 25mg over 2 mins (n=33)	**Primary:** Mean pain relief from baseline measured using a 100mm VAS at 0, 20, 40, 60, and 80 min	**Mean reduction from baseline to 80mins:** Haloperidol: 57mm ($p<0.01$)	Significant reduction from baseline NS when compared to each .05)
Roldan 2017, United States [28]	n=33	≥18 years	Abdominal pain with nausea and vomiting attributed to gastroparesis	IV haloperidol 5mg (n=15) With standard of care: (hydromorphone, metoclopramide, morphine, famotidine, pantoprazole, magnesium, lorazepam, promethazine)	IV placebo (n=18)	**Primary:** Mean reduction in 10-point VAS at 60 min	haloperidol: 5.37 vs. placebo: 1.11 ($p=0.11$)	Significant reduction, favoring haloperidol NS difference in standard of care received ($p>0.05$) No ADR in haloperidol group **Study did not meet power*

Table 4. Side Effects

Side Effect	Haloperidol (n = 31)		Metoclopramide (n = 33)	
	Baseline (Time 0) (%)	Developed AFTER Haloperidol (%)	Baseline (Time 0) (%)	Developed AFTER Metoclopramide (%)
Sleepiness*	25 (81)*	5 (16)	17 (52)*	9 (27)
Nausea	22 (71)	0 (0)	20 (61)	1 (3)

Alternative to opioids (ALTO) for different types of pain

Renal Colic


Renal Colic
Immediate / First Line Therapy
Ketorolac 15 mg IV
Lidocaine 1.5 mg/kg IV
Acetaminophen 1000 mg PO
Second Line - IV Therapy
Desmopressin 40 mcg intranasal

Opioid Naive Musculoskeletal Pain

Opioid Naive Musculoskeletal Pain

<u>Non-IV Therapy</u>

APAP 1000mg PO + Ibuprofen 600mg PO

Cyclobenzaprine 5mg PO or Diazepam 5mg PO

Gabapentin 300mg PO

Lidoderm Patch 4% or 5% (max 3 patches)

Trigger point injection with 1% Lidocaine

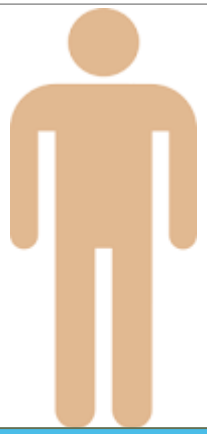
<u>Second Line - IV Therapy</u>

Ketorolac 15mg IV

Dexamethasone 8mg IV

Diazepam 5mg IV

Acute on Chronic Low Back Pain (Opioid Tolerant)



Opioid Tolerant Acute on Chronic Low Back Pain

<u>Non-IV Therapy</u>

APAP 1000mg PO + Ibuprofen 600mg PO

Cyclobenzaprine 5mg PO or Diazepam 5mg PO

Gabapentin 300mg PO

Lidoderm Patch 4% or 5% (max 3 patches)

Trigger point injection with 1% Lidocaine

<u>Second Line - IV Therapy</u>

Ketorolac 15mg IV

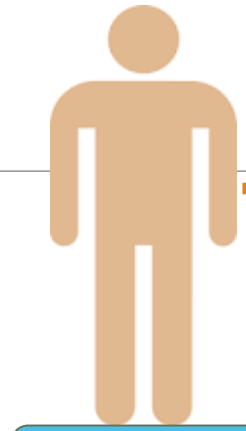
Ketamine 0.1-0.3 mg/kg IV over 10 mins

Ketamine 0.1 mg/kg/hour infusion

Dexamethasone 8mg IV

Diazepam 5mg IV

Headache/Migraine



Headache

Immediate / First Line Therapy

1L NS + 30mg Ketorolac IV
Metoclopromide 5-10mg IV
Acetaminophen 1000mg PO if applicable
Trigger point injection with 1% Lidocaine

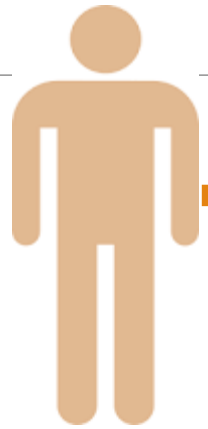
Alternative Options

Magnesium 1g IV over 60 minutes OR
Valproic Acid 500 mg over 20 mins OR
Dexamethasone 4-8 mg IV
Sumatriptan 6mg SC
Haloperidol 5mg IV

If Tension Component

Cyclobenzaprine 5mg or Diazepam 5mg PO
Lidoderm Patch 4% or 5% (max 3 patches)

Extremity Fracture / Joint Dislocation

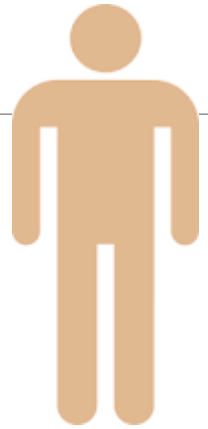


Fracture or Dislocation

<u>Immediate / First Line Therapy</u>
Ketamine 0.5 mg/kg IN (Max dose 50 mg; Max volume per nare 1 mL) APAP 1000mg and/or Ibuprofen 600mg Nitrous Oxide titrate up to 70%

<u>Ultrasound-guided Regional Anesthesia</u>
Disloc: Lidocaine 0.5 % peri-neural infiltration (max 5mg/kg) Fracture: Ropivacaine 0.5% peri-neural infiltration (max 3mg/kg)

Chronic Abdominal Pain



Chronic Abdominal Pain

<u>Immediate First-line Therapy</u>
1L NS Bolus
30mg Ketorolac IV
Metoclopromide 5-10mg IV
(or Prochlorperazine 5-10mg)
Diphenhydramine 25 mg IV

<u>Non IV Option (if applicable)</u>
Dicyclomine 20 mg PO/IM

<u>Second Line - Therapy</u>
Haloperidol 2.5-5 mg IV
Ketamine 0.1-0.3 mg/kg IV over 10 mins
Ketamine 0.1 mg/kg/hour infusion
Lidocaine 1.5 mg/kg (max 200 mg)

Implementation of an opioid-reduction process & policy

Policy Changes

- Procedural Sedation
  - Ketamine dosing – clearly define analgesia vs sedation doses
    - < 0.25 mg/kg slow IVP = analgesia
    - ≥ 1 mg/kg slow IVP = sedation = “timeout”
- High-Risk Medication Administration
  - Lidocaine administration
    - 1.5 mg/kg bolus over 10-60 min = non-ICU areas
    - Cardiac lidocaine = ICU
  - Ketamine administration
    - < 0.25 mg/kg slow IVP $\pm$ 0.1 mg/kg/hr x 48 hrs max = non-ICU areas
    - 1-2 mg/kg IV + 5-30 mg/hr = ICU

Pharmacy/IT Support

- Education
  - Nurses, physicians, pharmacists
- CPOE
  - Creation of pain treatment order set
  - Create order strings for unique entries – clearly label “for pain”

Pharmacy/IT Support

- Smart Pumps
  - Addition of new medications – clearly label “for pain”
    - Lidocaine
      - Bolus = 1.5 mg/kg in 100 mL NS over 10 min
    - Ketamine
      - Bolus = 50 mg/5 mL prefilled syringe entry to infuse over 10 min
      - Gtt = 100 mg/50 mL NS max 0.1 mg/kg/hr

Timeline for Success

3 months

- Medication Supply
  - Formulary additions/changes
  - Automated dispensing machines in ED
    - Stock all ALTO medications that you can
    - Individualized medications STAT from IP pharmacy

- Collaborate for optimization of administration policies for ALTO medications
  - ALTO ketamine/lidocaine - medical unit
  - Procedural sedation cutoffs for ketamine

3 months

- Data
  - Organization/system IT champion and data champion create order entries
    - Clearly labeled individual entries
    - Order set(s)

2 months

- Secure medication approval and stock medications in ED

• Ketamine	• Ketorolac
• Lidocaine Patches	• Capsaicin Topical
• Haloperidol	• Gabapentin

- Update smart pump medication libraries
  - Standard concentration
  - Dosage/indication
  - Max dose limits

- Educate pharmacy staff on ALTO therapies

Timeline for Success

1 month

- TEST RUN!!!
- All needed supplies/equipment ready
- Data Report
  - Run beta test report
  - IT/data champion look it over
  - Clinical Audit
    - Provider, pharmacist or nurse with great understanding of the ALTO medications and what should be appearing on the data report
    - Reporting only in mcg/mg/g?
    - No prepacks/discharge medications on report?
    - Note revisions/adjustments and work closely with IT/data champion to resolve

2 weeks

- Ensure smart pumps are updated and working
- Nurse education complete
- Provider education complete/questions answered
- Beta test data reports and audit again/issues resolved?
- Ensure stocking of medications is complete

Discharge medication list

Headache[12]:

For acute attacks:

- Sumatriptan 100 mg
- Acetaminophen/Aspirin/Caffeine (Excedrin Migraine)
- Acetaminophen 1000 mg every 6 hours
- DHE 2 mg nasal spray
- Naproxen 500-550 mg twice daily
- Metoclopramide 10 mg every 6 hours
- Ibuprofen 600 mg PO every 6 hours

For prevention:

- Propranolol 40 mg BID
- Divalproex DR 250 mg twice daily OR ER 500 mg daily
- Topiramate 25 mg at bedtime
- Magnesium supplementation 600 mg daily

Sore throat:

- Ibuprofen 600 mg every 6 hours
- Acetaminophen 1000 mg every 6 hours
- Dexamethasone 10 mg once
- Viscous lidocaine

Fibromyalgia[3,4]:

- Cardiovascular exercise
- Strength training
- Massage therapy
- Amitriptyline 10 mg at bedtime
- Cyclobenzaprine 10 mg every 8 hours
- Pregabalin 75 mg twice daily

Uncomplicated neck pain[5]:

- Acetaminophen 1000 mg every 6 hours
- Ibuprofen 600 mg every 6 hours
- Cyclobenzaprine 5 mg every 8 hours
- Physical therapy
- Lidocaine 5% patch Q12 hours

Uncomplicated back pain[6,7]:

- Acetaminophen 1000 mg every 6 hours
- Ibuprofen 600 mg every 6 hours
- Lidocaine 5% patch Q12 hours
- Diclofenac 1.3% patch TD twice daily
- Diclofenac 1% gel 4 g four times daily PRN
- Cyclobenzaprine 5 mg PO three times daily
- Heat
- Physical therapy
- Exercise program

Simple sprains:

- Immobilization
- Ice
- Ibuprofen 600 mg every 6 hours
- Acetaminophen 1000 mg every 6 hours
- Diclofenac 1.3% patch TD twice daily
- Diclofenac 1% gel 4 g four times daily PRN

(need more)[#]

Contusions[9]:

- Compression
- Ice
- Ibuprofen 600 mg *every* 6 hours
- Acetaminophen 1000 mg every 6 hours
- Lidoderm 5% patch

Non-traumatic tooth pain[10]:

- Ibuprofen 600 mg every 6 hours AND
- Acetaminophen 1000 mg every 6 hours
- *(clove oil, other topical anesthetics?)*

Osteoarthritis[11]:

- Diclofenac 50 mg every 8 hours
- Naproxen 500 mg twice daily
- Celecoxib 200 mg daily
- Diclofenac 1.3% patch TD twice daily
- Diclofenac 1% gel 4 g four times daily PRN
- *(topical NSAIDs, capsaicin?)*

Undifferentiated abdominal pain:

- Dicyclomine 20 mg every 6 hours
- Ibuprofen 600 mg every 6 hours
- Acetaminophen 1000 mg every 6 hours
- Metoclopramide 10 mg every 6 hours
- Prochlorperazine 10 mg every 6 hours

Neuropathic pain:

- Gabapentin 300mg at bedtime
- Amitriptyline 25 mg at bedtime
- Pregabalin 75 mg twice daily

References

1. Chumbley G. Use of ketamine in uncontrolled acute and procedural pain. Nursing Standard. 2010;25(15-17):35-7
2. Ketamine. Lexi-Drugs. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Available at: http://online.lexi.com. Accessed December 21, 2018.
3. Motov SM, Nelson LS. Advanced concepts and controversies in emergency department pain management. Anesthesiol Clin. 2016;34(2):271-85.
4. Sin B, Ternas T, Motov S. The use of subdissociative-dose ketamine for acute pain in the emergency department. Acad Emerg Med. 2015;22(3):251-7.
5. Sleigh J, Harvey M, Voss L, Denny B. Ketamine- more mechanisms of action than just NMDA blockade. Trends in Anaesthesia and Critcal Care. 2014;4:76-81.
6. Gurnani A, Sharma PK, Rautela RS, Bhattacharya A. Analgesia for acute musculoskeletal trauma: low-dose subcutaneous infusion of ketamine. Anaesth Intensive Care. 1996;24(1):32-
7. Majidinejad S, Esmailian E, Emadi M: Comparison of intravenous ketamine with morphine in pain relief of long bones fractures: a double blind randomized clinical trial. Emerg (Tehran). 2014;2(2):77-80.
8. Motov S, Rockoff B, Cohen V, Pushkar I, Likourezos A, McKay C, et al: Intravenous subdissociative-dose ketamine versus morphine for analgesia in the emergency department. Ann Emerg Med. 2015; 66(3):222-229,
9. Motov S, Mann S, Drapkin J, Butt M, Likourezos A, Yetter E, et al: Intravenous subdissociative-dose ketamine versus morphine for acute geriatric pain in the emergency department: a randomized controlled trial. Am J Emerg Med. 2018; pii:S0735-6757:30407-8.
10. Reynolds SL, Bryant K, Studnek J, Hogg M, Dunn C, Templin MA, et al: Randomized controlled feasibility trial of intranasal ketamine compared to intranasal fentanyl for analgesia in children with suspected extremity fractures. Soc Acad Emerg Med 2017;24(12):1430-1440.
11. Lidocaine. Lexi-Drugs. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Available at: http://online.lexi.com. Accessed December 21, 2018.
12. Motamed H, Maleki Verki M: Intravenous lidocaine compared to fentanyl in renal colic pain management; a randomized clinical trial. Emerg (Tehran) 5(1):e82, 2017.
13. Soleimanpour H, Hassanzadeh K, Vaezi H, Golzari SE, Esfanjani RM, Soleimanpour M: Effectiveness of intravenous lidocaine versus intravenous morphine for patients with renal colic in the emergency department. BMC Urol. 2012;12:13.
14. Acetaminophen. Lexi-Drugs. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Available at: http://online.lexi.com. Accessed December 21, 2018.
15. Ofirmev (Acetaminophen) [package insert]. Hazelwood, MO: Mallinckrodt; 2018.
16. Sinatra RA, Jahr JS, Reynolds LW, Viscusi ER, Groudine SB, Payen-Champenois C. Efficacy and safety of single and repeated administration of 1 gram intravenous acetaminophen injection (paracetamol) for pain management after major orthopedic surgery. Anesthesiology. 2005;102(4):822-31.
17. Bektas F, Eken C, Karadeniz O, Goksu E, Cubuk M, Cete Y: Intravenous paracetamol or morphine for the treatment of renal colic: a randomized, placebo-controlled trial. Ann Emerg Med. 2009;54(4):568-74.
18. Masoumi K, Forouzan A, Asgari Darian A, Feli M, Barzegari H, Khavanin A. Comparison of clinical efficacy of intravenous acetaminophen with intravenous morphine in acute renal colic: a randomized, double-blind, controlled trial. Emerg Med Int. 2014;2014:571326.

References

19. Azizkhani R, Pourafzali SM, Baloochestani E, Masoumi B. Comparing the analgesic effect of intravenous acetaminophen and morphine on patients with renal colic pain referring to the emergency department: a randomized controlled trial. J Res Med Sci. 2013;18(9):772-6.
20. Shams Vahdati S, Morteza Baghi HR, Ghobadi J, Rajaei Ghafouri R, Habibollahi P. Comparison of paracetamol (Apotel®) and morphine in reducing post pure head trauma headache. Anesth Pain Med. 2014;21:e14903.
21. Propofol. Lexi-Drugs. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Available at: http://online.lexi.com. Accessed December 21, 2018.
22. Drummond-Lewis J, Scher C. Propofol: a new treatment strategy for refractory migraine headache. Pain Med. 2002;3(4):366-9.
23. Soleimanpour H, Taheraghdam A, Ghafouri RR, Taghizadieh A, Marjany K, Soleimanpour M. Improvement of refractory migraine headache by propofol: case series. Int J Emerg Med. 2012;5(1):19.
24. Seidel S, Aigner M, Ossege M, Pernicka E, Wildner B, Sycha T. Antipsychotics for acute and chronic pain in adults. Cochrane Database Syst Rev. 2013;(8):CD004844.
25. Haloperidol. Lexi-Drugs. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Available at: http://online.lexi.com. Accessed December 21, 2018.
26. Sibley DR, Hazelwood LA, Amara SG. Sibley D.R., Hazelwood L.A., Amara S.G. Sibley, David R., et al.5-Hydroxytryptamine (Serotonin) and Dopamine. In: Brunton LL, Hilal-Dandan R, Knollmann BC. Brunton L.L., Hilal-Dandan R, Knollmann B.C. Eds. Laurence L. Brunton, et al.eds. *Goodman & Gilman's: The Pharmacological Basis of Therapeutics, 13e* New York, NY: McGraw-Hill; . http://0-accesspharmacy.mhmedical.com.liucat.lib.liu.edu/content.aspx?bookid=2189&sectionid=170105881. Accessed December 23, 2018.
27. Gaffigan ME, Bruner DI, Wason C, Pritchard A, Frumkin K. A Randomized Controlled Trial of Intravenous Haloperidol vs. intravenous metoclopramide for acute migraine therapy in the emergency department. J Emerg Med. 2015;49(3):326-34.
28. Roldan CJ, Chambers KA, Paniagua L, Patel S, Cardenas-Turanzas M, Chathampally Y. Randomized controlled double-blind trial comparing haloperidol combined with conventional therapy to conventional therapy alone in patients with symptomatic gastroparesis. Acad Emerg Med. 2017;24(11):1307-1314.

“We know of no other medication that kills so frequently”

Health care providers call to action,
V. Murthy, US Sugeon General
JAMA 2016

Questions?

Future Correspondence

Tran Tran, PharmD, BCPS

ttran@midwestern.edu

Billy Sin, PharmD, MBA, BCPS

billy.sin@mountsinai.org