Novel use of non-opioids for safe and effective acute pain management

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Objectives

1. List the principles for the use non-opioids for acute pain management

2. Discuss the advantages and disadvantages of various non-opioid agents

3. Identify supporting evidence for use of non-opioid alternatives

4. Describe the implementation of a practice centered on the use of non-opioids

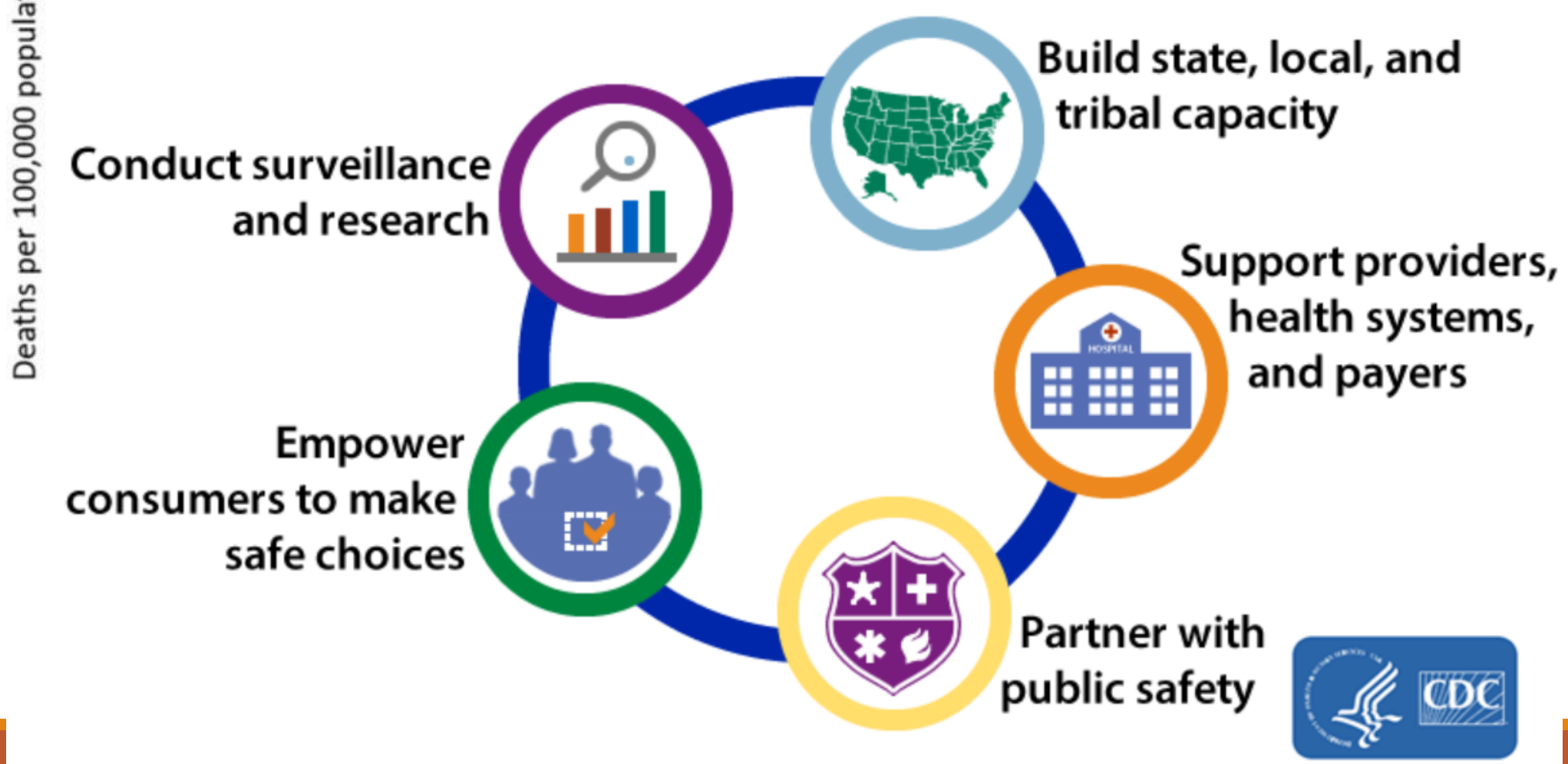
Poll

At my institution, the pharmacy department is actively involved in mitigating the use of opioids by working with interdisciplinary personnel (ie: nurses, doctors) on pain rounds or stewardship teams.

A. True

B. False

Preventing Opioid Overdoses and Related Harms



Principles for use of non-opioids

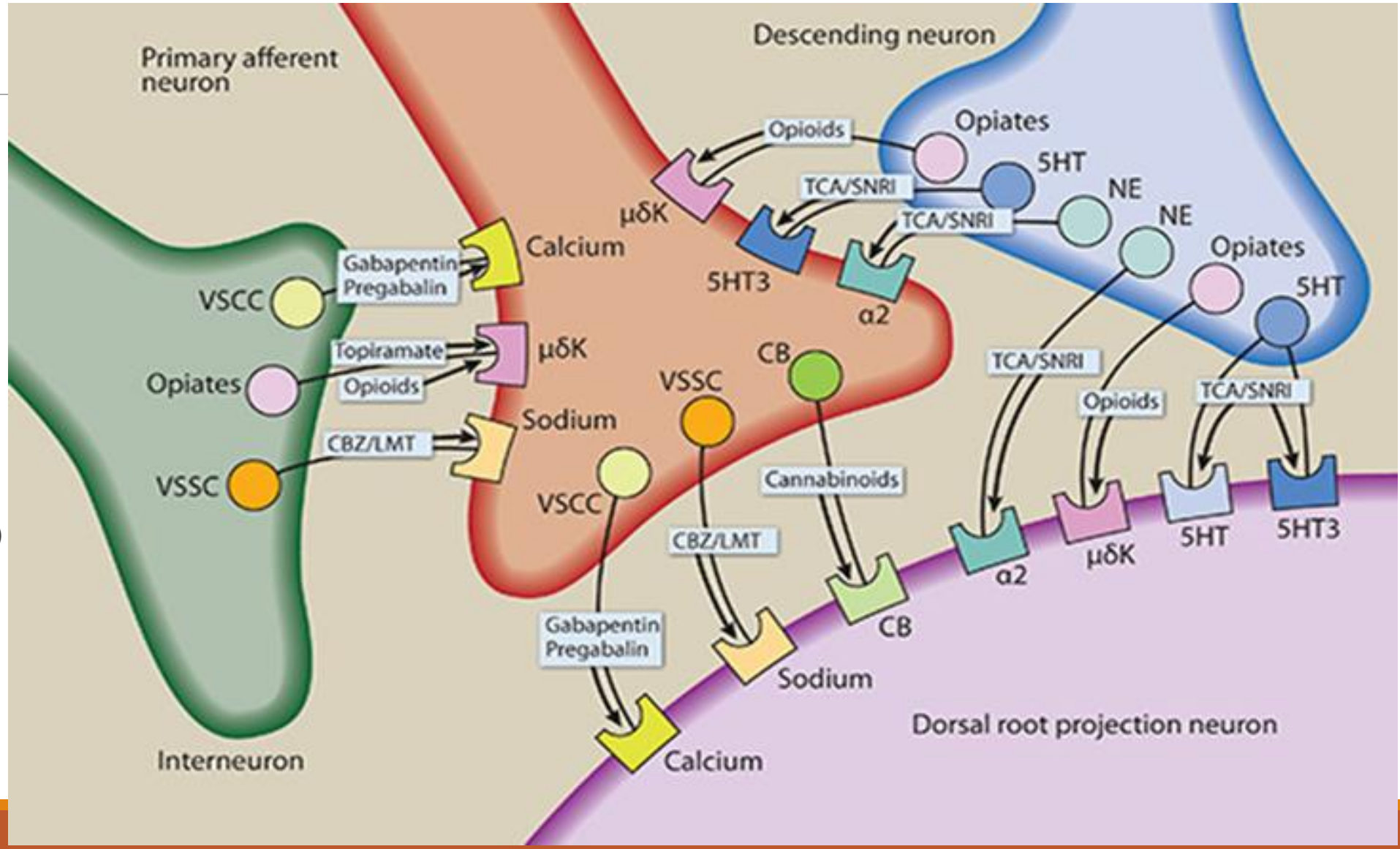
- Develop framework
  - Aim: Bed-side patient care
  - Implement process & procedure
  - Provide *continuous* education
  - Enhance the pharmacist-provider-patient relationship
- Identify & determine disease state
  - Targeted use of pharmacotherapy vs. pathophysiology
- Identify options
  - Channels, Enzymes, Receptors-Targeted Analgesia (CERTA)
  - Multimodal and holistic pain management

CERTA (Multimodal) approach[1]

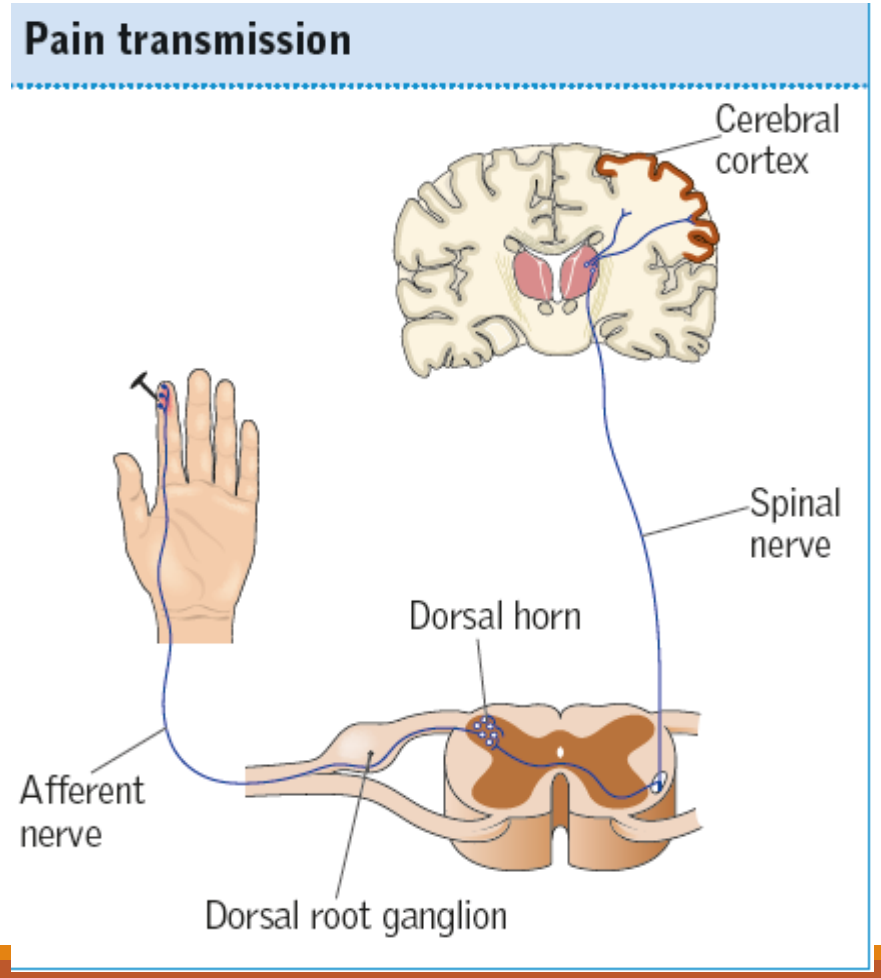
Channels:
- Sodium (Lidocaine)
- Calcium (Gabapentin)

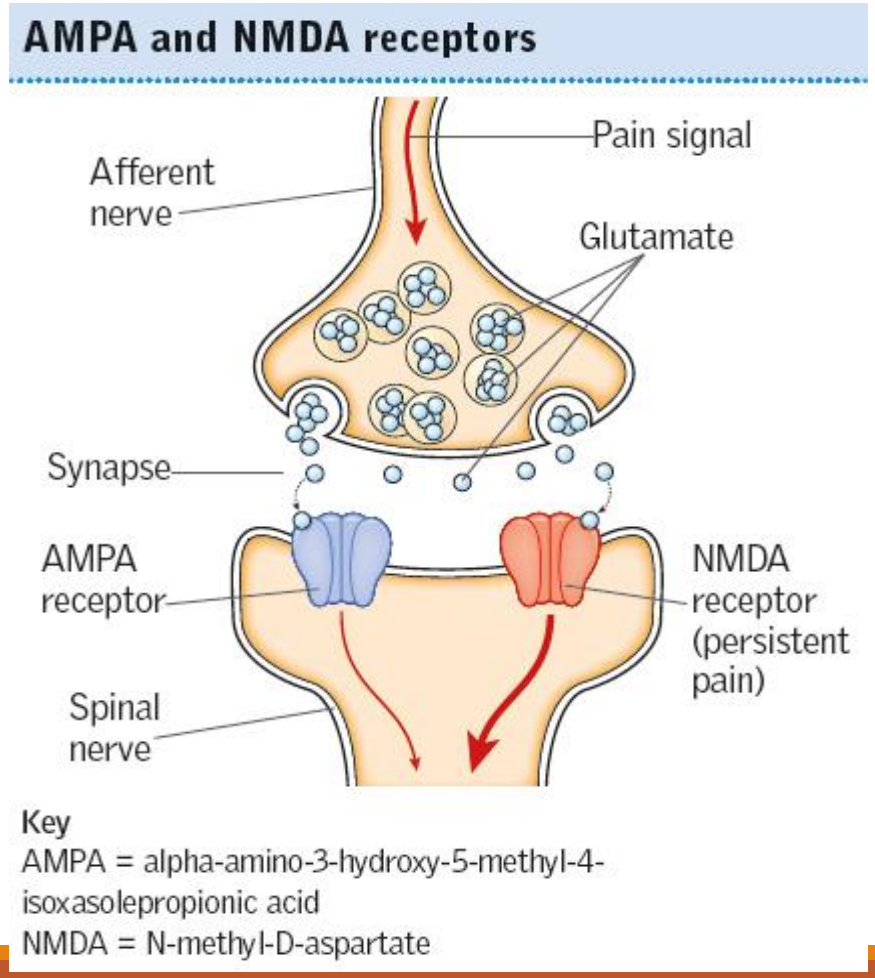
Enzymes:
- COX 1,2,3 (NSAIDS)

Receptors:
- MOP/DOP/KOP (Opioids)
- NMDA (Ketamine)
- GABA (Gabapentin/Sodium Valproate)
- $5HT_{1-4}$ (Haloperidol/Metoclopramide)
- D_{1-2} (Haloperidol)



Pain transmission via NMDA receptor[2]





Ketamine[2-4]

- **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

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.

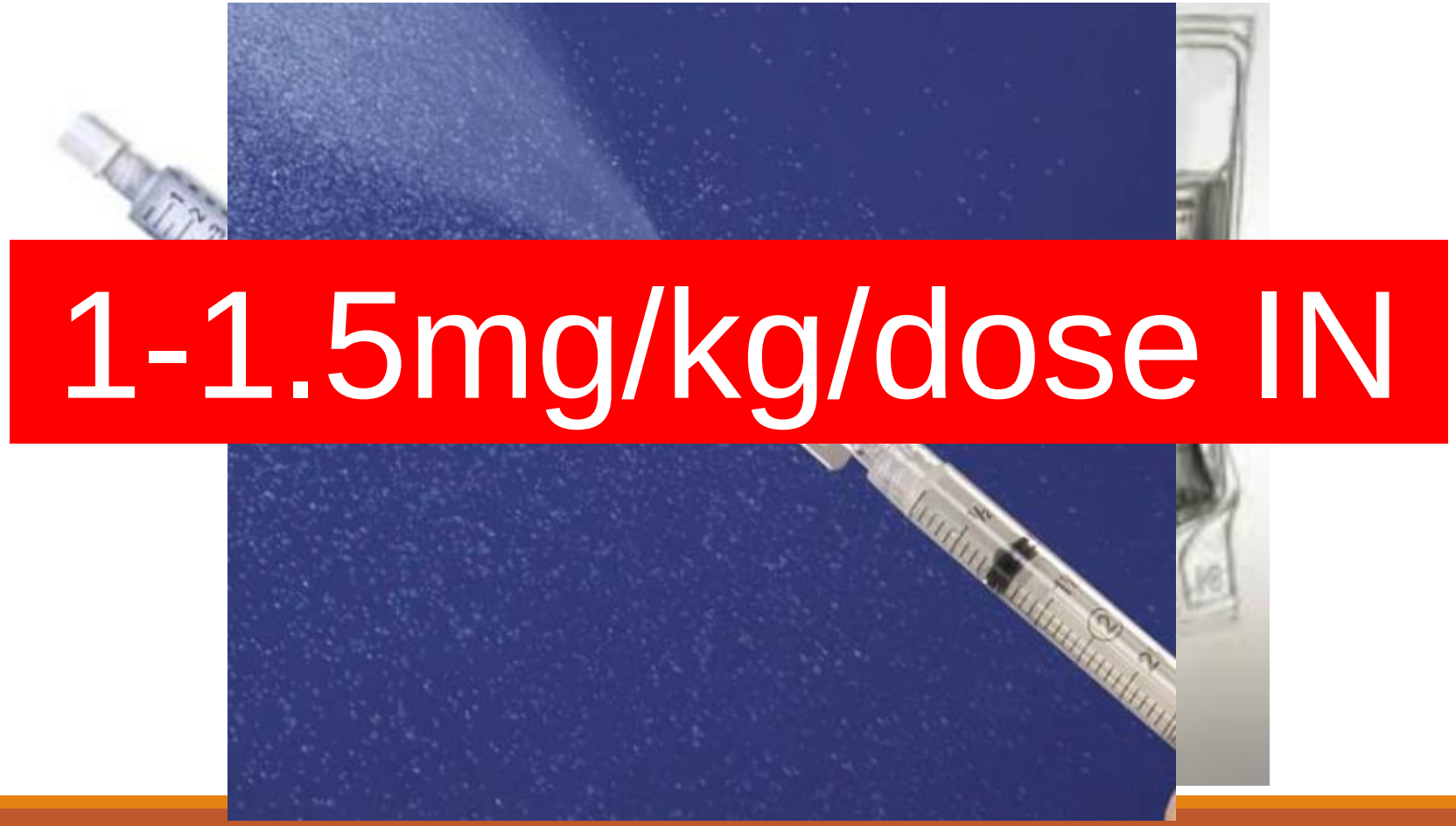
☐ **Keywords—acute pain; analgesia; subdissociative dose; ketamine**

Administration

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

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

Administration[1-4]



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


MAC
PC
Ket
bids
VS
XBOX
WHICH IS BETTER?

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?
  - How long will it take for procurement?
- Safety (Avoid in…)
  - Hemodynamic instability (high blood pressure)
  - Baseline psychiatric condition
  - Altered mental status

Which would you choose?

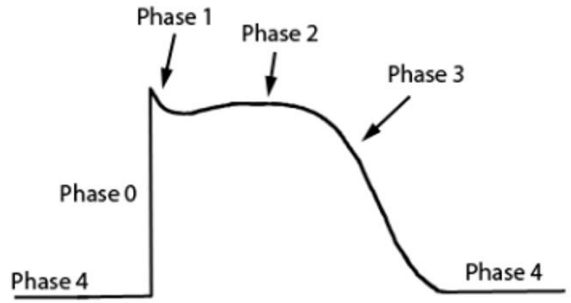
KK is a 45 year old male who presents to the ED with acute abdominal pain. The physician would like to initiate ketamine but would like to avoid potential nausea/vomiting. She inquires with you, the pharmacist, on whether ketamine should be administered as a push versus slow infusion over 10-15 minutes. Your response is….

A. Push

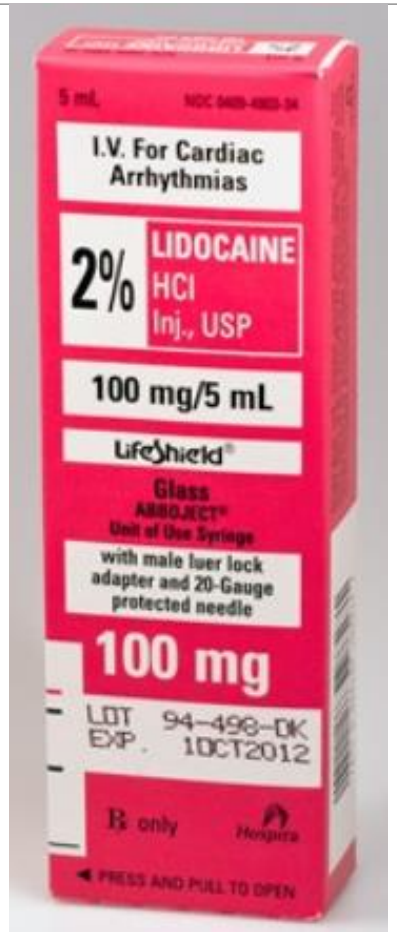
B. Infuse over 10-15 minutes

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


5 mL
I.V. For Cardiac Arrhythmias
2%
LIDOCAINE
HCl
Inj., USP
100 mg/5 mL
LifeShield
Glass
with male luer lock adapter and 20-Gauge protected needle
100 mg
LOT 94-498-DK
EXP. 10CT2012
℞ only
Hospira
PRESS AND PULL TO OPEN


20 mL
Multiple-dose
2%
LIDOCAINE HCl
Injection, USP
20 mg/mL

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-

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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
  - Literature does not mention cardiac monitor, but recommended
- Safety (Avoid in…)
  - Hemodynamic instability (electrolyte imbalance)
  - History of arrhythmia

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)

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

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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]	**IV Morphine** 0.1mg/kg 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]	**IV Morphine** 0.1mg/kg 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]	**IV Morphine** 0.1mg/kg 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?
- Already took something with Tylenol?
- Rate of infusion- over 15 minutes
- Safety (Avoid in…)
  - Hypersensitive
  - Liver dysfunction

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.

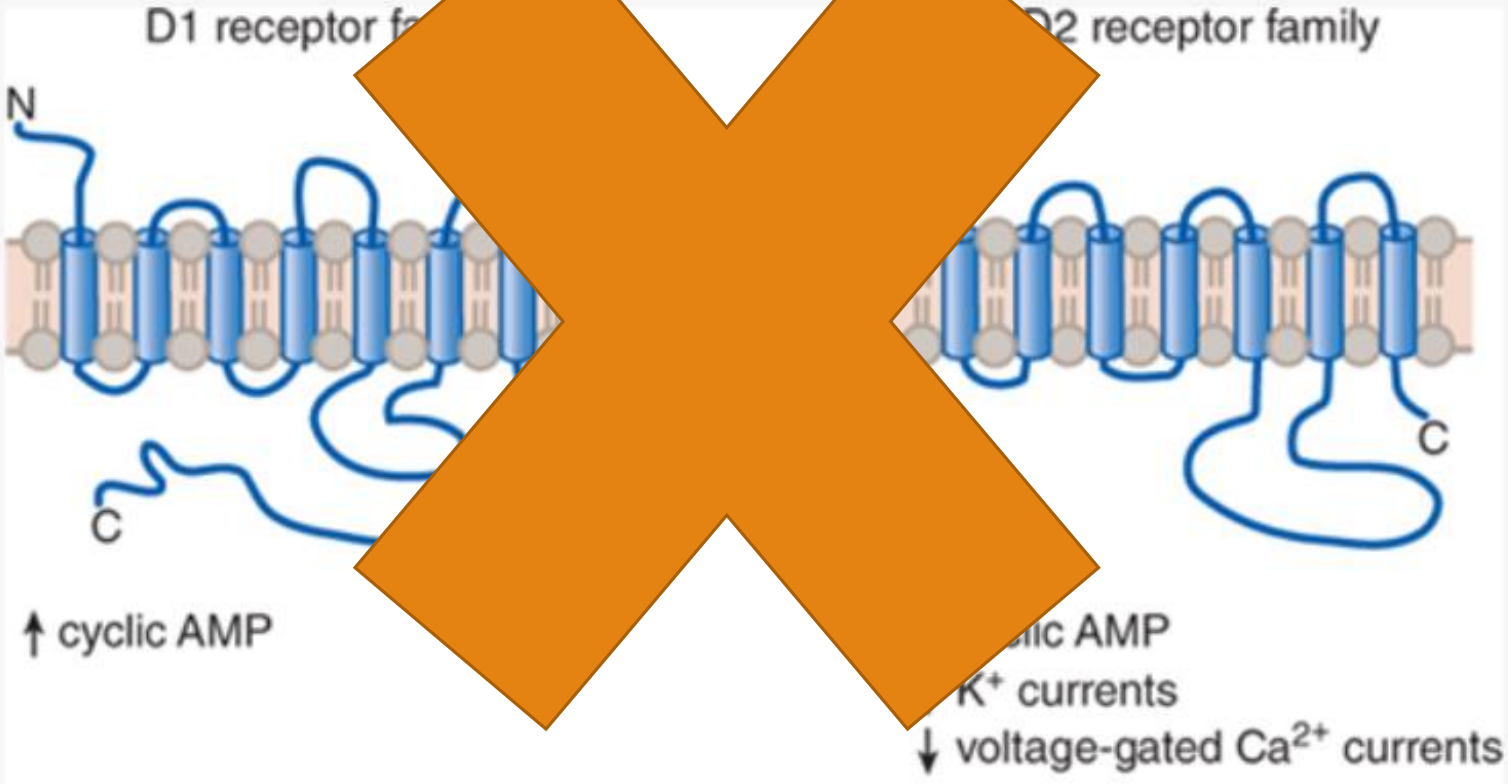
Discussion: It seems that in the treatment of intractable migraine headaches, GABAergic receptors, compared to the normal conditions, have a lower activity status.

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

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

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ORIGINAL CONTRIBUTION

CME

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

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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 [2	n=146	18-50 years	Migraine with at least (2 of following) 1. Unilateral location	IV haloperidol 5mg over 2 mins (n=31)	**IV metoclopramide** 25mg over 2	**Primary:** Mean pain relief from baseline measured using a	**Mean reduction from baseline to 80mins:**	Significant reduction from baseline
Roldan 2017, United States [28]	n=33	≥18 years	Abdominal pain with nausea and vomiting attributed to gastroparesis	IV haloperidol 5mg (n=15)	**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*
				With standard of care: (hydromorphone, metoclopramide, morphine, famotidine, pantoprazole, magnesium, lorazepam, promethazine)				

Table 4. Side Effects

	Haloperidol (n = 31)		Metoclopramide (n = 33)	
Side Effect	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)
Restlessness	10 (32)	10 (32)	13 (39)	4 (12)
Chest pain	0 (0)	2 (6)	2 (6)	0 (0)

Test your knowledge

AK is a 24 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: 122/92, 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 is the best recommendation for AK?

A. Acetaminophen

B. Ketamine

C. Propofol

Systematic approach to implementation

1. Identify interdisciplinary champions (6 months before “go-live”)
   - Build trust: “Prove it to me”, start with one case
   - Gaining Support
   - “What’s in it for them”: improve outcomes, publications, financial incentive for institution?
2. Review current practices (5 months before “go-live”)
   - “What are we doing today”
     - Avoid: “We have been doing this for years”, “This is the way that has been done”
   - What medication is used (why?)
   - Identify outcomes for improvement
   - “Are there gaps in: process, IT (CPOE), practice norms, availability/shortages?

Systematic approach to implementation

3. Identify the role of the pharmacist (5 months before “go-live”)
   - Aim: Leading expert in pharmacotherapy use
     - Education, education, education
     - Design patient specific pharmacotherapeutic care plan
     - Bedside monitoring & counseling
     - Member of the providing team
4. Identify tools available to achieve goal (5 months before “go-live”)
   - CPOE & Smart pumps
     - Order sets/pathways
     - Therapy specific monitoring parameters
     - Dosages, warnings (hard-stop, soft-stop), concentrations

Systematic approach to implementation

5. Meet with interdisciplinary personnel & executive leadership (4 months before “go-live”)
   - Justify practice model & campaign for resources
   - Implement IT changes to CPOE/smart pumps/order sets
   - Arrange & coordinate inventory
   - Test-run (1 month before go-live)
6. Data collection (suggested duration: 3 months)
   - Obtain data to determine impact of practice
   - “Manage up” patient stories and experiences
   - Advertise practice in the community

Summary

1. Principles for the use non-opioids include: providing bedside patient care, continuous education, and recommending variety of pharmacologic options

2. Utilize the advantages and avoid disadvantages of each agent

3. Emerging literature supporting the use of non-opioids are available

4. Implementation of a medication use policy involve phases of planning, implementing, and monitoring

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