KETAMINE:

TRADITIONAL UNDERSTANDINGS AND NEW INSIGHTS FOR USE

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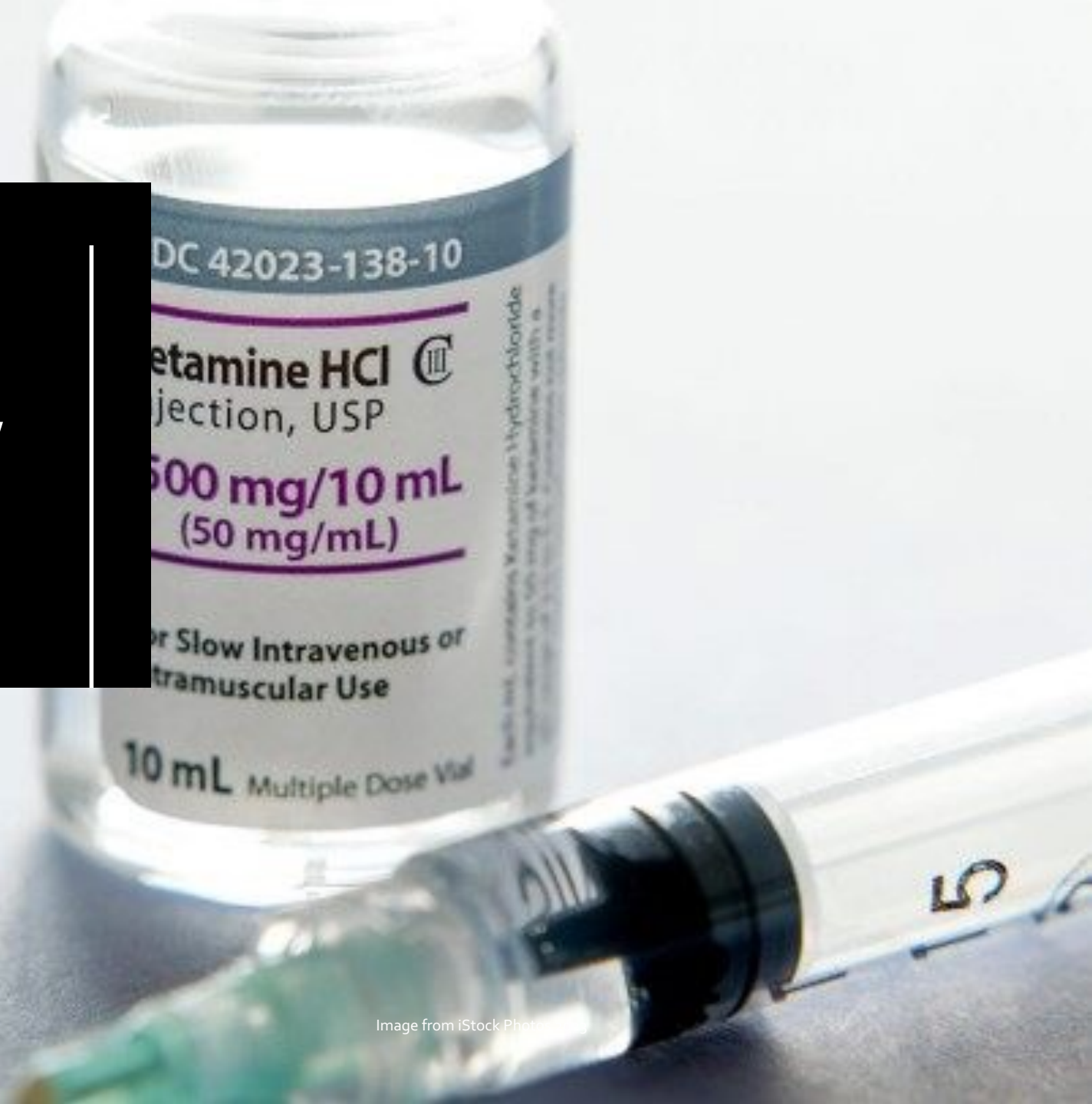

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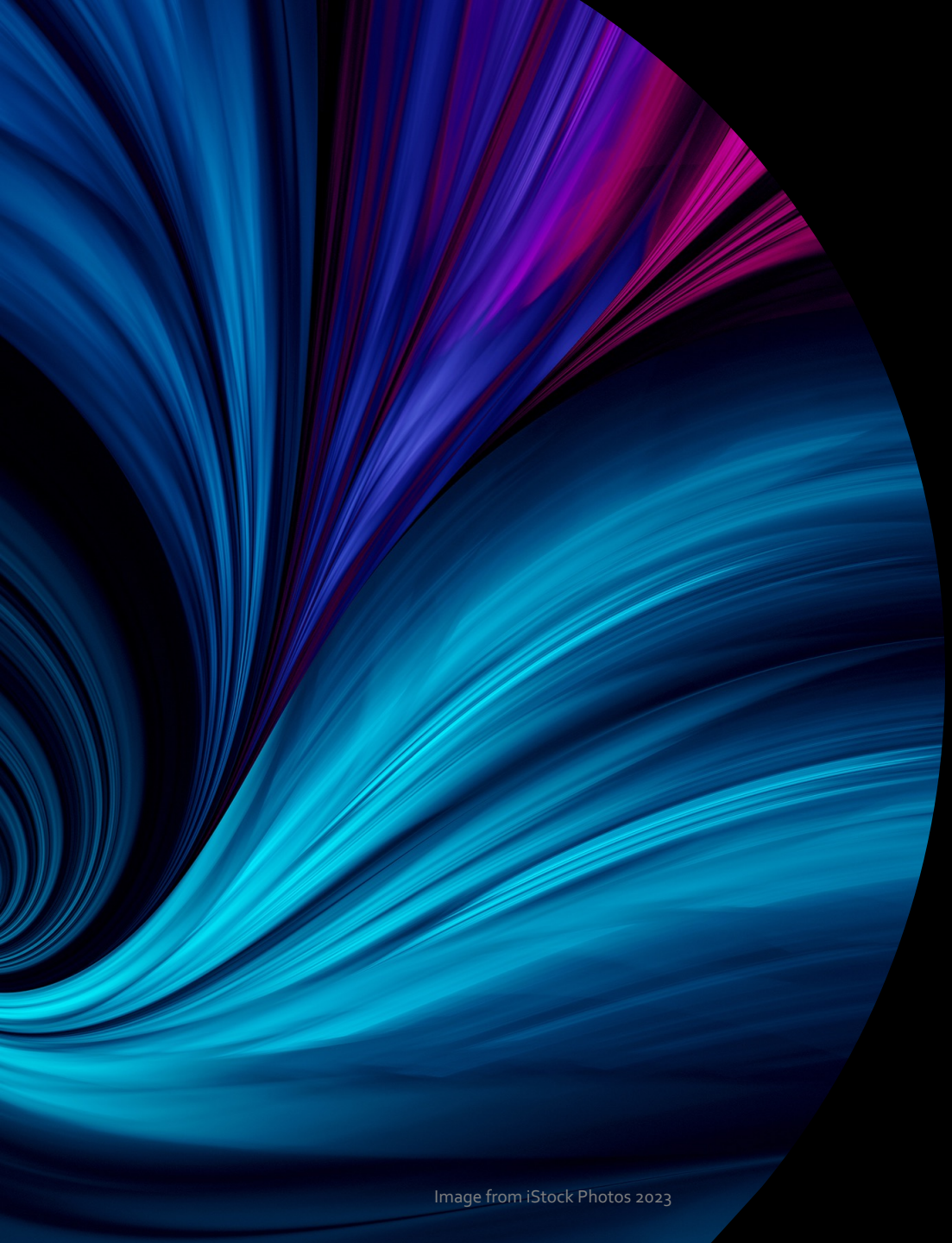
Objectives

1. Define indications and potential benefits of utilizing ketamine in the ICU, stepdown, and med surg units for adjunct pain control.
2. Explain pharmacokinetics for ketamine's unique therapeutic effects.
3. Define indications and dosing strategies for pain, analgosedation, and intubation.
4. Identify considerations of ketamine administration including identification and management of dissociative effects.
5. Discuss safety, monitoring, and other nursing implications for patients receiving high dose ketamine.



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DOWN INTO THE K-HOLE

What is your role?

a) I am a bedside RN

b) I am an APRN who prescribes

c) I am an APRN but do not prescribe

d) Neither

Does your institution use Ketamine in the ICU?

a) Yes

b) No

Does your institution use Ketamine outside the ICU or in Non-intubated patients?

a) Yes

b) No

c) Rarely / I’ve heard rumors but never seen it

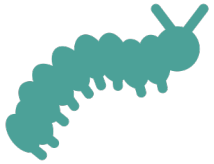
Are you pumped for this talk??

a) Take me to the K-hole

b) Sedate me now

What is **Ketamine**?

Ketamine is a schedule III controlled substance



Medication Class:

Rapid-acting General Anesthetic

Phencyclidine (known as PCP) derivative hypnotic and analgesic

What does it look like?

Colorless, odorless liquid

Illegally ketamine can be a smooth white powder or tablet

Definitions

- Anesthetic dosing
- Subanesthetic dosing
- High dose
- Low dose
- Emergence reactions
- Dissociation

History of Ketamine

- Street Use
  - Ketamine became popular as a psychedelic drug in 1960's
  - Became preferred over PCP, as it acts faster
  - 1980's became a party drug and began to dominate raves
  - 2000's became less popular as heroin and cocaine took off
  - *Long term ketamine abusers may report cystitis and urinary tract problems (Wieruszewski et al, 2016)

History of Ketamine

- Medical Use
  - Discovered in 1962, tested on animals and prisoners
  - Approved by FDA in 1970, first used in American soldiers during the Vietnam War
  - 1999 became a federally controlled substance
  - Since ketamine has **less respiratory suppression** than most other anesthetics, it has been widely used for safety induction and maintenance of general anesthesia in humans as well as animals.
  - Recent research has shown unique benefits of ketamine in chronic and acute pain management, status asthmaticus, treatment resistant depression, PTSD, and status epilepticus

Sidebar:
How is Ketamine abused?

- Abuse of the drug gained popularity when users discovered that it produced effects like PCP.
- Has psychologic and physiologic dependence
- Used as a date rape drug
- Can be smoked or ingested
- Street names for ketamine include “K,” “Special K,” “Vitamin K,” and “Cat Tranquilizer.” (Li, et al, 2011)

Sidebar:
Is Ketamine chronically addictive?

- While ketamine is not physically additive, it can produce heavy psychological dependence, like cocaine
- Prolonged ketamine abuse may cause memory loss, damage to other brain functions, and kidney and bladder damage

(Li, et al, 2011)

Image from iStock Photos 2023

What does "dissociative" mean?

- AKA "emergence phenomenon" or "psychotropic effects"
- Distorts perceptions of sight and sound and produces feelings of detachment from the environment and self.
- Deprives the CNS of outside stimuli such as pain, sight and sound which results in a trancelike state (Li & Vlisides, 2016)
- Low doses result in impaired attentions, learning ability, and memory
- At higher doses, causes dreamlike states and hallucinations
- Can also cause delirium and amnesia at high doses

Image from iStock Photos 2023

Benefits

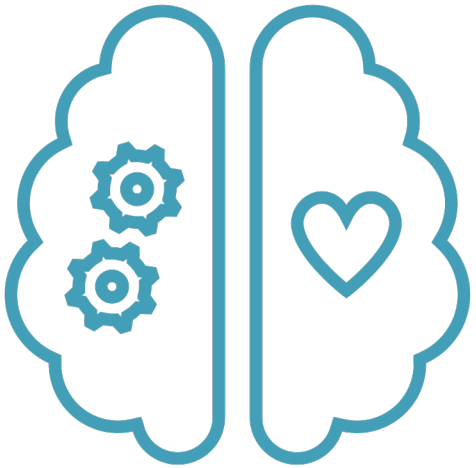
- Analgesia, anesthesia
- Decreases use of other analgesics and/or sedatives
- No respiratory depression, Decreases bronchospasm
- Does not cause hypotension or bradycardia
- May decrease vasopressor requirements
- Does not negatively impact GI motility
- Quick onset
- Currently, no data to show increase in delirium
- Few contraindications
- Potential for reduction in depression

Risks

Why Not?

- May cause hypertension, tachycardia, and emergence reactions
- Many uses not FDA approved, so some hesitancy
- Not ideal for all populations
- Limited prospective studies

Pharmacokinetics



- Lipid Soluble
  - Crosses the blood-brain barrier
  - Quick onset of action in IV form
  - Rapid recovery to baseline in IV form
- Metabolized in the liver, excreted by the kidneys
- Elimination half-life is **1-2** hours in children and **2-3** hours in adults, since it distributes into the peripheral tissues

(Ketamine, 2021)

Pharmacokinetic Properties

Bioavailability:

IV/IO	**100%**
Intramuscular	**93%**
Intranasal	**50%**
Oral	**20-25%**

Onset

Intramuscular	3-4 min
IV	Immediate
Intranasal	10 min
Oral	5-20 min

Half-life

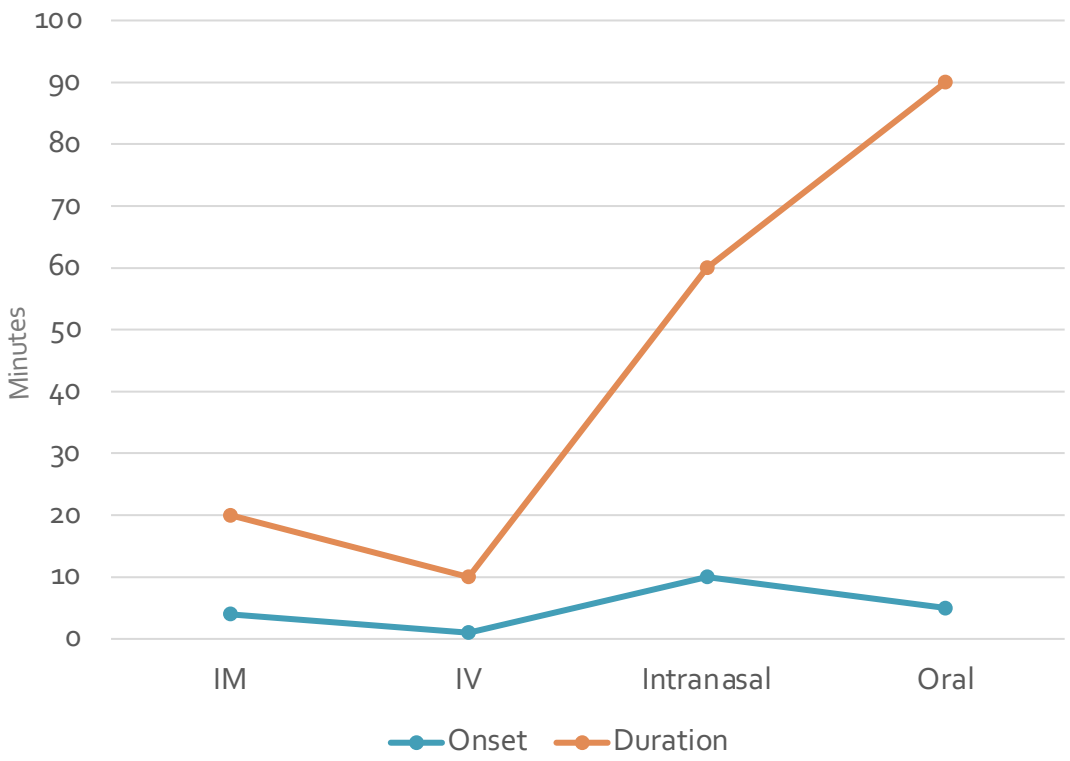
Distribution	10 min
Elimination	2-3 hr*

Duration

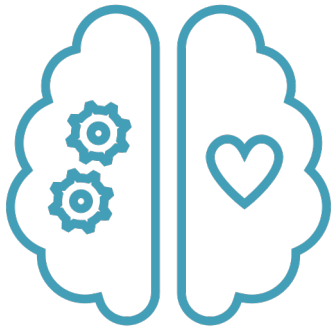
Intramuscular	12-25 min
IV	5-10 min
Intranasal	60 min
Oral	90 min

Metabolism/Elimination

- Hepatic
- Excretion (urine 91%, stool 3%)



Mechanism of Action



- NMDA glutamate receptor blocker → resulting in dissociative, analgesic, and neuroprotective effects
- Opioid receptors → analgesic effects and dysphoric effects
- Muscarinic receptors → partial antagonist effect (bronchodilation, sympathomimetic, delirium)
- Na+ channel blocker→ causes mild local anesthetic like properties
- Inhibition of norepinephrine/serotonin reuptake → psychomimetic and sympathomimetic effects (Aleksandrova et al, 2017)

Rapid Effects

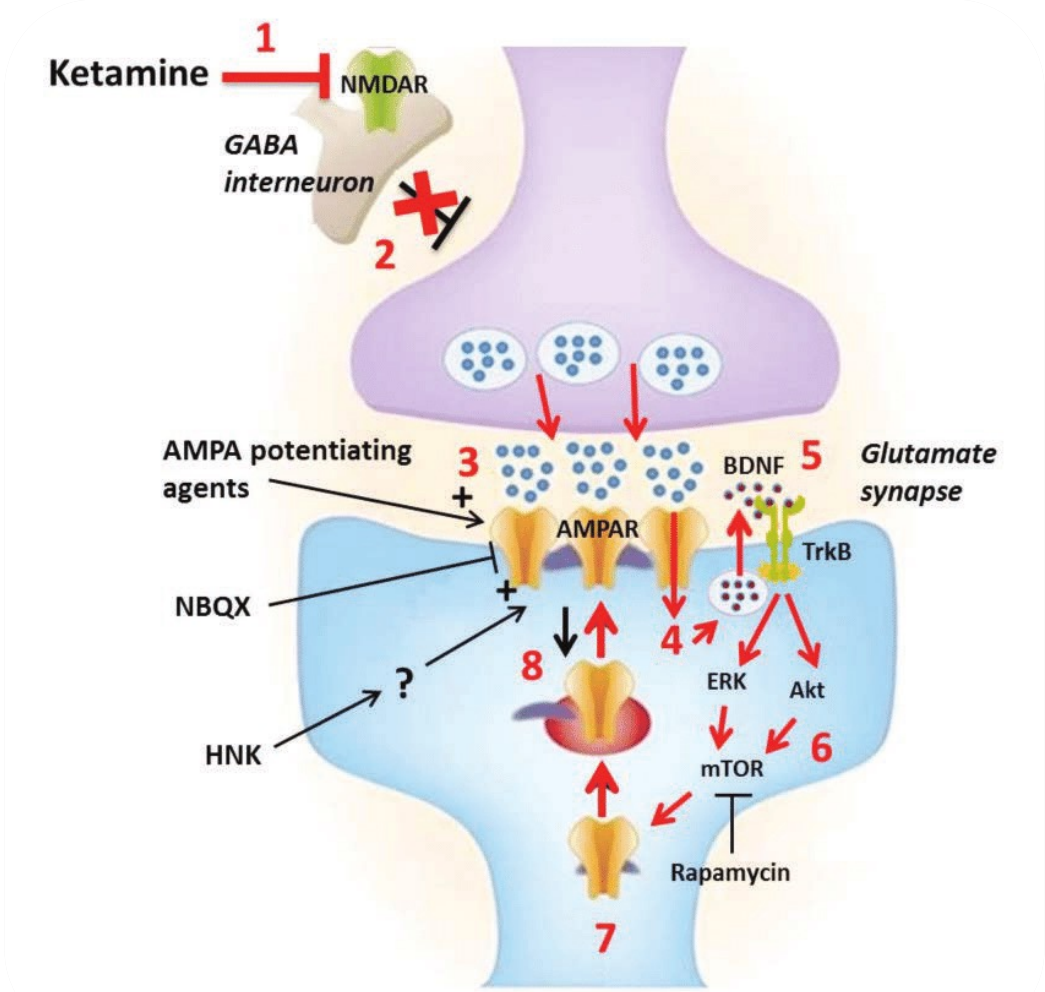
- Opiate Receptors
- Glutamate Receptors

Sustained Effects

- NMDA receptors
- Glutamate Receptors

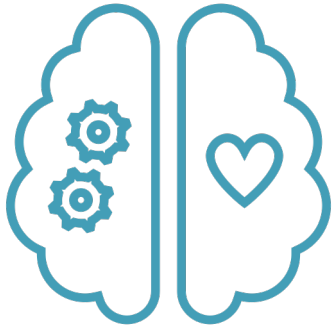
Return to baseline

- New neural receptors formed



(Aleksandrova, et al, 2017)

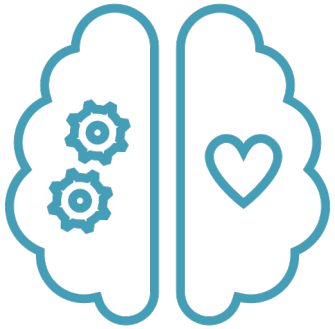
Dose Dependent Effects



- ✓ **CNS** (even low) → mild dissociation, distortion of time and space, analgesia, euphoria
- ✓ **CNS** (high doses) →complete dissociation, hallucinations, amnesia, analgesia, euphoria
- ✓ **CV** (all doses) → sympathomimetic stimulation → hypertension, tachycardia, increased salivation
- ✓ **CV** (higher doses >20mg/kg) →direct myocardial depressant in the setting of catecholamine depression
- ✓ **Resp** (all doses) → NO respiratory depression, bronchodilation
- ✓ **Resp** (low doses) → may stimulate respiration

(Aleksandrova et al., 2017)

Ketamine Side Effects



Cardiovascular (usually with boluses)

- Hypertension (can be treated with clonidine, call MD)
- Tachycardia
- Increased myocardial oxygen demand
- Increased cardiac output

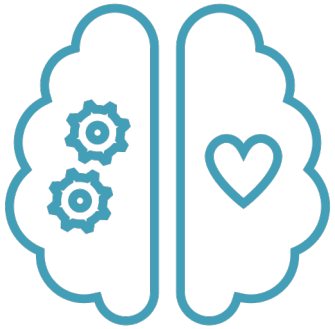
Respiratory

- Bronchodilation
- Laryngeal spasms

Endocrine

- Hypersalivation (treat with glycopyrrolate)
- Nausea and vomiting *(rare)*
- Cholangiopathy *(rare)*

Side Effects Cont…



CNS Psychologic Side Effects

- Hallucinations, agitation, vivid dreams
- Misperceptions, misinterpretations, illusions
- Euphoria, excitement, confusion or fear
- Emergence psychosis

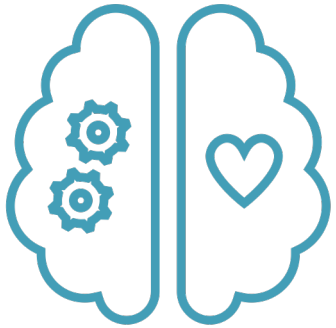
**Benzodiazepines may be used to treat agitation, vivid dreams and prevent emergence reactions. Ativan is recommended for extreme agitation*

CNS Physiologic Side Effects

- Petit mal seizure-like activity
- Dilated pupils and nystagmus
- Non-purposeful coordinated movements

(Orhurhu et al, 2021)

Contraindications



Relative

- PAH, liver disease, heart failure, acute MI, stroke HTN, renal failure, patients that will not tolerate sympathetic nervous system activation, psychosis, pregnancy

Absolute

- Known hypersensitivity to ketamine
- Uncontrolled ACS

Ketamine Myths Busted

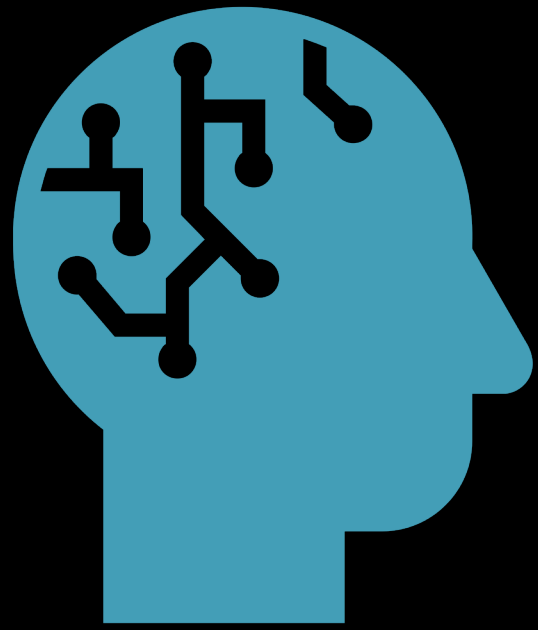


Table 1: Definition of Low vs. High Dose Intravenous and Intramuscular Ketamine

Regimen	Low Dose*	High Dose*
IM injection or IVPB bolus	0.1-0.35 mg/kg	>0.35 mg/kg
Continuous infusion	0.1-1 mg/kg/hr	>1 mg/kg/hr

*For comparison, anesthesia induction dose = 0.5-2 mg/kg and maintenance dose = 1-4 mg/kg/hr.

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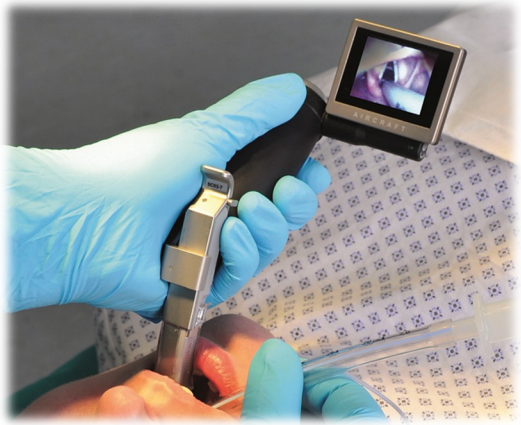
Ketamine Indications

1) RSI
2) Procedural Sedation
3) Status Asthmaticus
4) Status Epilepticus
5) Severe Agitation
6) Chronic Pain
7) Acute Pain
8) Analgosedation

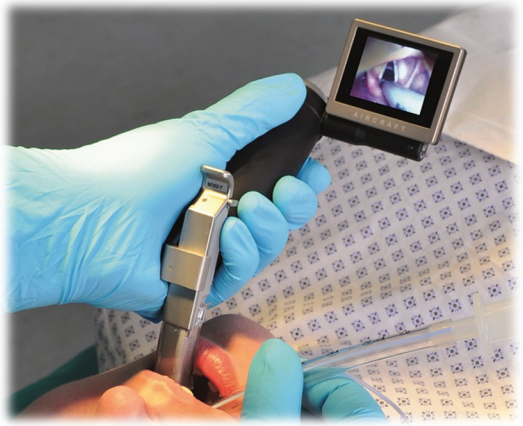
Rapid Sequence Intubation



- **RSI**
  - **Considered in patient with bronchospasm or hemodynamic compromise**
  - **IVP:** Initial: **1 to 2 mg/kg once over 1 minute;**
  - in patients with shock, use 1 mg/kg.
  - **IO: 100 mg once**

(Ketamine, 2021)

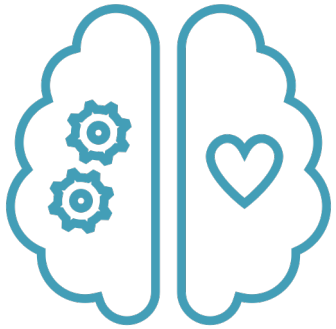
Procedural Sedation



- **To reduce emergence reactions, may premedicate with benzo**
- **IVP:** Initial: **1 to 2 mg/kg over 1 to 2 minutes.**
  - repeat dose (0.5 to 1 mg/kg) every 5 to 10 minutes; use lower doses (0.25 to 0.5 mg/kg) depending on concomitant sedation and clinical status.
- Some experts use 0.5 to 0.75 mg/kg (as a 1:1 mixture) when combined with propofol.

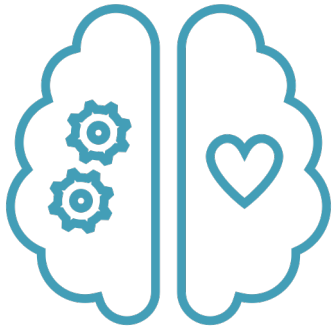
(Ketamine, 2021)

Status Asthmaticus



- **Not enough data for recommendation, but several clinical case reports**
- **Mostly used in children, although not routinely used**
- **May be tried as an adjunct**
- **IV:** loading dose **0.5 mg/kg to 1 mg/kg** followed by infusion of **0.13-3 mg/kg/hr**
- **Give SLOWLY**

Status Epilepticus



- **When other therapies have failed**
- **Requires mechanical ventilation, and continuous EEG is recommended**
- **24 hrs of burst suppression recommended before down titrating**
- **IV:** Initial: **1.5 mg/kg or 0.5 to 3 mg/kg;** repeat loading dose of 0.5 mg/kg every 3 to 5 minutes as needed for electrographic/burst suppression, followed by continuous infusion

  Continuous Infusion: **0.1 – 4 mg/kg/hr, max dose 15 mg/kg/hr**

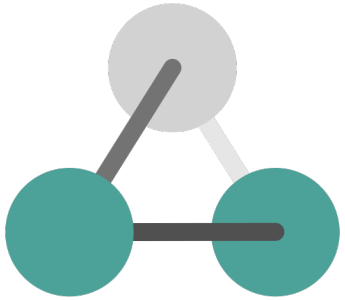
(Hofler, 2016)

Severe Agitation

- **Rare usage**
- **When benzos and/or antipsychotics have failed**
- **IVP:** Initial**: 1 to 2 mg/kg once over 30 to 60 seconds**; if initial sedation is inadequate,
  - may repeat dose once 5 to 10 minutes after the initial dose using 0.5 to 1 mg/kg; however, this is not common if using the upper end of the initial dose range.

(Ketamine, 2022)

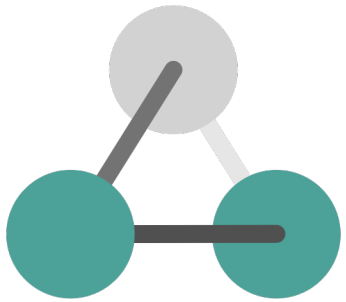
Ketamine for Pain Control



- **Ketamine has been shown effective in treating abdominal, back, neuropathic, post-operative, headache, musculoskeletal, burn and sickle cell pain**
- **Chronic and acute pain** (or acute-on-chronic)
- **Ketamine's effects are dose-dependent**
  - Low doses are used for analgesia-bolus and infusion, less likely to cause dissociation and psychiatric side effects.

(Cohen et al, 2018)

Surgical Pain



- **Practice Guideline for Ketamine in Total Joint Arthroplasty (2022)**
- Recommends Ketamine be administered **intraoperatively**
  - Decreases post op opioid consumption
  - Strong recommendation
  - Not associated with adverse events

CHRONIC AND INTERVENTIONAL PAIN

SPECIAL ARTICLE

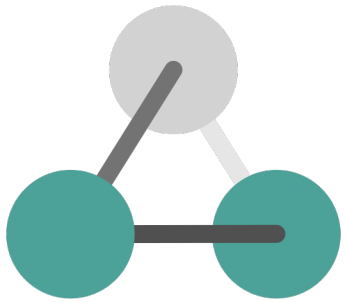
OPEN

Consensus Guidelines on the Use of Intravenous Ketamine Infusions for Chronic Pain From the American Society of Regional Anesthesia and Pain Medicine, the American Academy of Pain Medicine, and the American Society of Anesthesiologists

Steven P. Cohen, MD,† Anuj Bhatia, MBBS, MD,‡ Asokumar Buvanendran, MD,§ Eric S. Schwenk, MD,||*
*Ajay D. Wasan, MD, MSc,** Robert W. Hurley, MD, PhD,†† Eugene R. Viscusi, MD,||*
*Samer Narouze, MD, PhD,‡‡ Fred N. Davis, MD,§§|||| Elspeth C. Ritchie, MD, MPH,***†††*
Timothy R. Lubenow, MD,§ and William M. Hooten, MD‡‡‡

(Cohen et al, 2018)

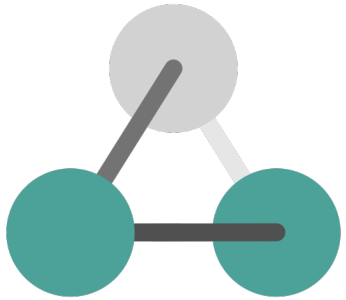
Chronic Intractable Pain



- **Must have a pain, palliative care, or anesthesia consult**
- **IV intermittent infusion:** Initial: **0.25 to 0.6 mg/kg** (usual maximum dose: 60 mg) as a 4- to 6-hour infusion
- **IV continuous infusion:** Initial: **0.05 to 0.15 mg/kg/hr** for 2 to 5 days inpatient; titrate to pain goal and tolerability; usual dosing range: **0.02 to 1 mg/kg/hr**
- **SubQ:** ?
- **Oral:** Initial: **0.5 mg/kg/day** administered in 3 to 4 divided doses as needed; then increase dose in increments of ~5 mg
  - **dose** based on pain goal and tolerability; maximum daily escalation dose: 15 to 20 mg; maximum dose: 800 mg/day.

(Cohen et al, 2018)

Acute Pain



- **In and out of ICU**
- **Must have a pain, palliative care, or anesthesia consult**
- Mod-severe pain not responding to other modalities / opioid tolerant
- **IV:** Initial: **0.25 to 0.5 mg/kg** bolus (maximum bolus: 35 mg), followed by **0.1 to 0.5 mg/kg/hr** continuous infusion in patients who need a longer duration of analgesia; titrate to pain goal and tolerability; duration of infusion: 48 to 72 hours
- **Intranasal: 0.2 to 1 mg/kg** by administering half dose in each nostril (using 100 mg/mL solution); if necessary, may repeat after 10 to 15 minutes with 0.25 to 0.5 mg/kg; titrate to pain goal and tolerability.

(Cohen et al, 2018)

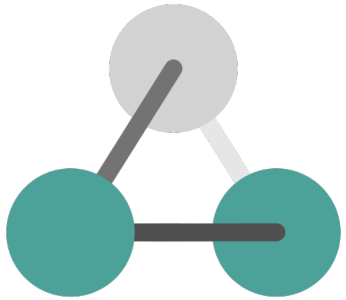
Intranasal ketamine

Image from iStock Photos 2023

- The injectable formulation is used to make intranasal doses.
- Concentration is 100 mg/mL
- May be administered undiluted or diluted in normal saline to a concentration of 20 mg/mL.
- Administer half of dose in each nostril using a needleless syringe or mucosal atomizer device.
- *Efficacy does not differ between routes*

(Ketamine, 2021)

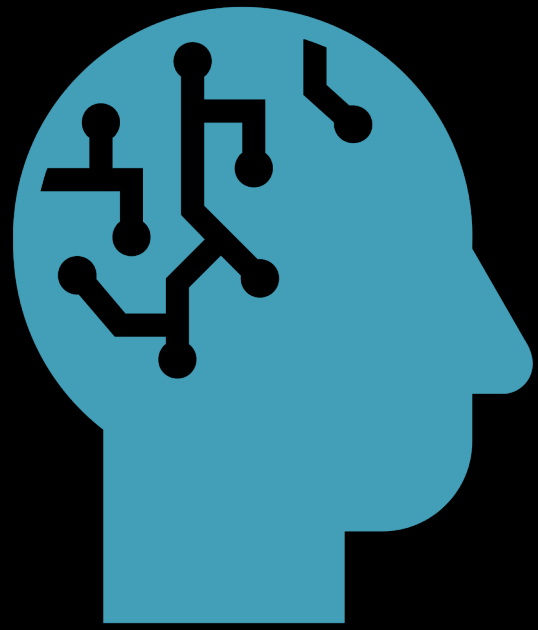
Analgosedation



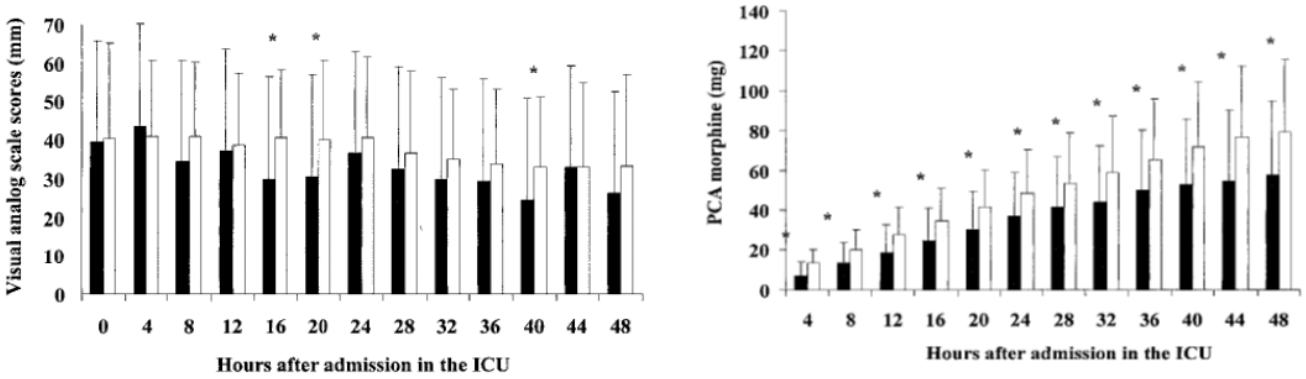
- **As an adjunct**
- **IV:** Initial: **0.1 to 0.5 mg/kg** bolus (maximum bolus: 35 mg), followed by **0.05 to 1 mg/kg/hr** continuous infusion in patients who need a longer duration of analgesia;
  - may need to use doses at the higher range in patients who are opioid-tolerant or with opioid-induced hyperalgesia; duration of infusion: 48 to 72 hours
- Titrate every 30 min
- Use caution in presence of poorly controlled hypertension, heart failure, or MI
- Watch HR

(Cohen et al, 2018)

Sidebar: Does Ketamine fit in the PAD-IS Guidelines?



Adjunctive Low-dose Ketamine in Surgical ICU Patients



Single center, prospective, randomized, double blind trial including 93 patients scheduled to have major abdominal surgery and post-op management and ventilation in the SICU. Patients were randomized to receive morphine PCA with either placebo or ketamine (for 48 hours). Both groups were allowed as needed morphine boluses.

Guillou N, et al. Anesth Analg 2003; 97:843-847

Considerations:

- Only one RCT available (with a very high risk of bias)
- Data limited to abdominal surgery patients only
- Safety (particularly delirium) not reported
- Role of sedation on effect unclear
- Builds on considerable observational data in non-ICU post operative populations

Society of Critical Care Medicine
The Intensive Care Professionals

Right Care Right Now.

"We suggest using low-dose ketamine (0.5 mg/kg IVP x 1, 1-2 mg/kg/hr) as an adjunct to opioid therapy when seeking to reduce opioid consumption in post-surgical adults admitted to the ICU (conditional, low quality of evidence)"

(Devlin et al, 2018)

Case Study R.R

- RR presents to ED with 10/10 abdominal pain, N/V
- Hx: neuropathy, HL, OSA, recent PNA, IV drug use on methadone, drinks 1 6-pack/ wk, marijuana use
- Dx: pancreatitis
- Poor pain/sedation management, requiring increasing dose of multiple agents
  - Dex
  - Fentanyl
  - Midazolam
  - Propofol
- Hemodynamically unstable- pressors on/off

- FURTHER COMPLICATIONS
  - Developed pneumonia
  - Acute respiratory distress syndrome (ARDS)

- Day 4 Patient still fighting the ventilator despite:
  - Dexmedetomidine @ 1.5mcg/kg/hr (MAX)
  - Fentanyl @ 250 mcg/hr
  - Midazolam @ 20 mg/hr
  - Propofol @ 40 mcg/kg/min

- STARTED ON NIMBEX DRIP
- Patient is proned.

- Triglycerides = 738 mg/dL

- Sedation increased
  - Propofol weaned to 20 mcg/kg/min
  - Midazolam @ 40 mg/hr
  - Fentanyl titrated to 400 mcg/hr
  - Dexmedetomidine @ 1.5 mcg/kg/hr
- Methadone re-started 40 mg TID

- Attempts to wean propofol failed
- Midazolam @ 60 mg/hr
- Attempts to wean fentanyl failed
- Dexmedetomidine stopped

- Now what?

- Described by MD as “difficult to sedate”

- Nurse asks pharmacist, what about Ketamine?
- Ketamine given
- 1 mg/kg loading dose (= 120 mg)
- 8-64 mcg/kg/min (0.48-3.84 mg/kg/hr)
- May increase in intervals of up to 8 mcg/kg/min q 1-2 hrs to achieve BIS of 45-60.
- Ketamine titrated up to 20 within 12 hrs
- MD progress notes
  - **“After adequate sedation his oxygenation issues seemed to improve significantly”**

Image from Microsoft PowerPoint 2022

- Patient on ketamine ~3 days
- Titrated up to 60 mcg/kg/min *(3.6mg/kg/hr)*
- Medications during ketamine infusion
  - Fentanyl @ 300 mcg/hr
  - Methadone 40 mg TID
  - Midazolam 20-50 mg/hr
- Day 5 - Ketamine stopped
- Day 6 - Patient appeared well enough for extubation

Burn Patients

Legacy Oregon Burn Center. Legacy Oregon Burn Center Burn Care Website. Legacy Oregon Burn Center | Legacy Health

- **McGuiness and colleagues (2011) found statistically significant reduction in pain as a primary analgesic**
- **Particularly helpful in dressing changes (less resp suppression)**
- **Lots of ongoing research**
  - As an adjunct for pain/sedation
  - Adjunct during dressing changes/ procedural sedation
  - VR and Ketamine during dressing changes

(Cohen et al, 2018)

Image from Microsoft PowerPoint 2022

Case Study E.C.

- E.C. admitted on 3/4/23 s/p tent fire from propane accelerant
- Hx of meth use, heroin, ??
- Medical history unknown
- 60% burns to arms, hands, neck, trunk, high, calves
- s/p allograft 3/6
- Plan of care: dressing changes daily to arms legs, doner sites to dry out
- Challenges of extreme rigidity

Image from Microsoft PowerPoint 2022

- Prior to dressing change at 1315, administered 100 mg IV Ketamine, CPOT 3
- 2 mg Versed 1320 RASS +1
- Another 100 mg IV Ketamine, 2 versed 1345 due to extreme rigidity (agitation), RASS +3, CPOT 4
- Medication response within 2 minutes: CPOT 1, Rass -1

Image from iStock Photos 2023

Implications and Monitoring

When should I consider Ketamine for my patient?

- Think about using ketamine if…
  - Opioids are not tolerated due to allergy or adverse effects
  - Opioids alone are ineffective for managing pain
  - Opioids are not wanted by the patient/provider
    - previous or current heroin or opioid addiction, chronic opioid use
  - Unstable hemodynamics where hypotension or respiratory depression would not be tolerated
  - Intractable pain
  - Opioid shortages

Prior to Initiating Ketamine

- Prior to initiation note their Vitals
  - BP and HR especially
  - Are they on an inotrope?
  - Can their heart handle it?
  - Are they catecholamine depleted?
  - Are oral secretions a problem?
- Understand WHY we are starting Ketamine
  - Decrease sedation or propofol for BP? Heavy opioid requirement?
  - Second line for agitation?
- Decide what you are looking for upon initiation
  - What are you expecting to see?
  - Partial vs total dissociation
  - Baseline CPOT and RASS
  - Sympathetic changes?

How to Manage a Ketamine drip

- Plan for bolus + maintenance dosing
- Start at **0.1 to 0.5 mg/kg** bolus (maximum bolus: 35 mg), followed by **0.05 to 1 mg/kg/hr**
- Titrate every 30 min, although onset is immediate
- Check in on your patient- effects/side effects
- Example: Patient who is 89 kg has a 0.2 mg/kg bolus followed by .05 mg/kg/hr infusion will receive a 17.8mg bolus over 15 min, then maintenance dose
- Program pump for bolus and infusion
- Plan to titrate, Begin to titrate down other sedatives or analgesics
- Plan ahead- pharmacy has to mix this

Patient Monitoring

*Review prior opioid administration because ketamine can potentiate the effects of opioids

- Document vitals q15 min including RASS and CPOT upon initiation, then q4h
- BP, HR, RR
- Continuous SpO2 or end tidal CO2
- Assess pain per policy
- Increased secretions
- Observe for psychiatric symptoms/ emergence reactions
- Observe for side effects
- *Ensure patient is alert and tolerating PO after ketamine is discontinued

Route of Administration	Dose Initiation or Increase	Maintenance
Enteral	HR, RR, BP, LOC^ hourly for 4 hours	Per unit standard
Intranasal	HR, RR, BP, LOC^ hourly for 4 hours	Per unit standard
Parenteral	**Low Dose**	**High Dose**
Continuous infusion	Continuous pulse oximetry or end tidal CO_2 monitoring; continuous cardiac monitoring; and RR, BP and LOC^ hourly x4 following initiation or dose changes and then every 4 hours once stable infusion dose achieved	Continuous pulse oximetry or end tidal CO_2 monitoring; continuous cardiac monitoring; and RR, BP and LOC^ hourly x4 following initiation or dose changes and then every 4 hours once stable infusion dose achieved
IM	HR, RR, BP, LOC^ every 15 minutes x4 then per unit standard	HR, RR, BP, LOC^ every 15 minutes x4 then every 30 minutes x2, then per unit standard
IVPB bolus	HR, RR, BP, LOC^ every 15 minutes x4 then per unit standard	HR, RR, BP, LOC^ every 15 minutes x4 then every 30 minutes x2, then per unit standard

Monitoring Parameters

Bedside Nursing Considerations

- Patient and family education!
- If IVP, slow over 1 minute
- Provide a dark, quiet area for recovery
- Minimize physical and sensory stimulation (if possible)
- Close to nurses station
- Plan to wean opioids
- Prepare for emergence reactions and monitor closely upon initiation

Hospital ICU Protocols

- **NEW YORK STATE PARTNERSHIP FOR PATIENTS**
  - Adult ICU Pain and Sedation Guideline for Mechanically Ventilated Patients
    - Opioid tolerance
    - Status asthmaticus/COPD
    - Hemodynamic instability
  - Bolus: 1.5 mg/kg
  - Infusion: 0.75-3 mg/kg/hr
    - Titrate 0.25 mg/kg/hr q 1 hr
    - Max: 3 mg/kg/hr

Hospital ICU Protocols

- **ST DOMINIC-JACKSON MEMORIAL HOSPITAL**
  - Ketamine Sedation Protocol for Emergency and Critical Care
    - Mechanically ventilated
    - Alternative to propofol/midazolam for patients with hypotension and/or bradycardia
  - Bolus: 0.5—1 mg/kg/hr
  - Infusion:0.1-1 mg/kg/hr with usual range between 0.1-4.5 mg/kg/hr
    - Titrate by 0.25-0.5 mg/kg/hr q 30 minutes

Hospital ICU Protocols

- **MICHIGAN MEDICINE**
  - Ketamine IV Continuous Infusion Guidelines for Mechanically Ventilated Adult ICU Patients
    - ICU attending approval
    - Also for status asthmaticus, alcohol withdrawal, status epilepticus, pain (consult pain service)
  - No bolus
    - Infusion: 0.2-1.2 mg/kg/hr
      - Titrate by 0.1 mg/kg/hr q15 minutes

Hospital ICU Protocols

- **LEGACY HEALTH GUIDELINE FOR KETAMINE ADMINISTRATION**
  - Chronic or acute pain
  - As an adjunct for pain/sedation in ICU
  - Burn patients
  - Suggest having a benzo available PRN
  - Can be given in and outside the ICU
    - RNs should have ACLS for infusions
    - End of Life exceptions
  - Very specific dosing orders available per indications
  - ICU sedation
    - Bolus: 0.1 mg/kg
    - Infusion: 0.25-2 mg/kg/hr
    - Titrate by 0.12 mg/kg/hr q15

Areas of Emerging Research

1) **Treatment Resistant Depression**
2) **PTSD**
3) **AWS**
4) **Addiction**

Treatment Resistant Depression

- Provides relief from depression in about **50-70%** of patients
- Inpatient dose 0.05 mg/kg single infusion over 40 min. Up to 1mg/kg
- Effects can last several days to a few weeks
- No sex differences in antidepressant response or tolerability
- For outpatients, IV route is a barrier
- Esketamine was granted FDA approval in March 2019

- *Lots of ongoing research in in youth*
- *No biomarkers identified in systematic revies and meta-analyses*

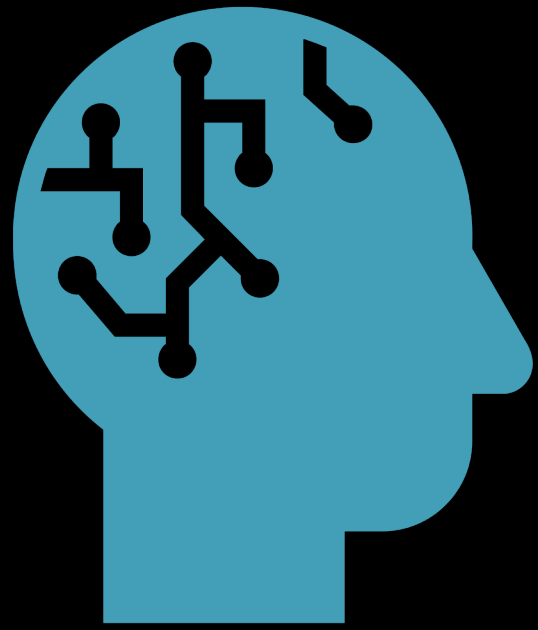
(Daly, et al, 2018)

PTSD

- **Lots of case reports of improvements in behavior after IV ketamine.**
- **Some studies done using one IV infusion, with results lasting for weeks**
- **30 patients – 15 received Ketamine**
- 6 IV infusions compared with Midazolam
- Stopped early due to clear benefit
- **Ketamine may "rewrite maladaptive memories"**
  - Were the participants thinking about their traumas when receiving this therapy??
- More research needed

(Feder et al, 2021)

Sidebar:
Is there a role for Ketamine in the prevention of PICS?



Alcohol Withdrawal Syndrome

- A systematic review by Garel et. Al (2022) reviewed **1922** abstracts with a total sample size **692** patients
- 5 studies reviewed impact of ketamine in alcohol use disorder in out patient settings
- 3 studies reviewed the effect of adding ketamine to conventional treatment in patients in the ICU
- Mixed results
- Most promising results in outpatient settings
- More research needed

Addiction

- **Cocaine addiction**
  - Single low dose Ketamine infusion combined with mindfulness-based behavioral training
  - 55 patients in cocaine study
  - 1 dose IV ketamine in 5 day hospital stay
  - 5 week course of mindfulness-based relapse prevention therapy
  - *Ketamine compared with placebo significantly increased likelihood of abstinence
- **Study was repeated in Alcohol addicted patients and heroin addiction**

(Dakwar et al, 2019)

Resources

- AACN
- SCCM
- Consensus Guidelines on The Use of IV Ketamine
- Ketamine Training
- State Board Scope of Practice

THANK YOU!

Enjoy the rest of the conference!

References

1. Aleksandrova, L.R., Philips, A.G., & Wang, Y.T. (2017). Antidepressant effects of ketamine and the roles of AMPA glutamate receptors and other mechanisms beyond NMDA receptor antagonism. Journal of Psychiatry and Neuroscience: JPN, 42(2), 160-75. hrrps://doi.org/ 10.1503/jpn.160175
2. Cohen, S. P., Bhatia, A., Buvanendran, A., Schwenk, E. S., Wasan, A. D., Hurley, R. W., Viscusi, E. R., Narouze, S., Davis, F. N., Ritchie, E. C., Lubenow, T. R., & Hooten, W. M. (2018). Consensus Guidelines on the Use of Intravenous Ketamine Infusions for Chronic Pain From the American Society of Regional Anesthesia and Pain Medicine, the American Academy of Pain Medicine, and the American Society of Anesthesiologists. Regional anesthesia and pain medicine, 43(5), 521–546. https://doi.org/10.1097/AAP.0000000000000808
3. Daly, E. J., Singh, J. B., Fedgchin, M., Cooper, K., Lim, P., Shelton, R. C., ... Drevets, W. C. (2018). Efficacy and safety of intranasal esketamine adjunctive to oral antidepressant therapy in treatment-resistant depression: A randomized clinical trial. JAMA Psychiatry, 75, 139-148.
4. Dakwar, E., Nunes, E. V., Hart, C. L., Foltin, R. W., Mathew, S. J., Carpenter, K. M., Choi, C. J. "Jean," Basaraba, C. N., Pavlicova, M., & Levin, F. R. (2019). A Single Ketamine Infusion Combined With Mindfulness-Based Behavioral Modification to Treat Cocaine Dependence: A Randomized Clinical Trial. American Journal of Psychiatry, 176(11), 923–930. https://doi-org.lhs.idm.oclc.org/10.1176/appi.ajp.2019.18101123
5. Devlin JWSY, Skrobik Y, Gélinas C. , et al. (2018). Clinical practice guidelines for the prevention and management of pain, agitation/sedation, delirium, immobility, and sleep disruption in adult patients in the ICU. Crit Care Med 2018; 46 (09) e825-e873
6. Feder A, Costi S, Rutter SB, et al. (2021). A randomized controlled trial of repeated ketamine administration for chronic posttraumatic stress disorder. Am J Psychiatry 2021; 178:193–202

References

7. Garel, N., McAnulty, C., Greenway, K. T., Lesperance, P., Miron, J. P., Rej, S., Richard-Devantoy, S., & Jutras-Aswad, D. (2022). Efficacy of ketamine intervention to decrease alcohol use, cravings, and withdrawal symptoms in adults with problematic alcohol use or alcohol use disorder: A systematic review and comprehensive analysis of mechanism of actions. *Drug and alcohol dependence*, *239*, 109606. https://doi.org/10.1016/j.drugalcdep.2022.109606
8. Hofler J, Rohracher A, Kalss G, et al. (S)-Ketamine in refractory and super-refractory status epilepticus: a retrospective study. CNS Drugs. 2016;30(9):869–876.
9. Ketamine (2021). UpToDate. Retrieved March 29, 2021 from https://www.uptodate.com/contents/ketamine-drug-information?source=see_link
10. Legacy Health Ketamine Administration Policy 2019.
11. Li, J.-H., Vicknasingam, B., Cheung, Y.-W., Zhou, W., Nurhidayat, A. W., Jarlais, D. C. D., & Schottenfeld, R. (2011). To use or not to use: an update on licit and illicit ketamine use. Substance Abuse And Rehabilitation, 2, 11–20. https://doi.org/10.2147/SAR.S15458
12. Li, L., & Vlisides, P. E. (2016). Ketamine: 50 Years of Modulating the Mind. Frontiers in human neuroscience, 10, 612. https://doi.org/10.3389/fnhum.2016.00612
13. Liriano, F., Hatten, C., & Schwartz, T. L. (2019). Ketamine as treatment for post-traumatic stress disorder: a review. Drugs in context, 8, 212305. https://doi.org/10.7573/dic.212305
14. McGuinness, S. K., Wasiak, J., Cleland, H., Symons, J., Hogan, L., Hucker, T., & Mahar, P. D. (2011). A systematic review of ketamine as an analgesic agent in adult burn injuries. Pain Medicine (Malden, Mass.), 12(10), 1551–1558. https://doi-org.lhs.idm.oclc.org/10.1111/j.1526-4637.2011.01220.x
15. Orhurhu VJ, Vashisht R, Claus LE, et al. Ketamine Toxicity. [Updated 2020 Nov 15]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK541087/
16. Wieruszewski, P. M., Leung, J.G., Nelson, S. (2018). Ketamine use in the intensive care unit. AACN Advanced Critical Care, 29(2), 101-108.