Utilization of Ketamine for Pain, Excited Delirium, and Procedural Sedation in the Emergent Setting

Daniel Yousef, Pharm.D.
Emergency Medicine Clinical Specialist
Residency Program Director, PGY-2 Emergency Medicine
Jackson Memorial Hospital

Disclosure

- I do not have (nor does any immediate family member have):
  1. a vested interest in or affiliation with any corporate organization offering financial support or grant monies for this continuing education activity
  2. any affiliation with an organization whose philosophy could potentially bias my presentation

Objectives

- Describe the use of ketamine for acute pain in the emergency department
- Review the use of ketamine for excited delirium in the pre-hospital setting and emergency department
- Discuss the role of ketamine in procedural sedation and rapid sequence intubation
- Select an appropriate dosing regimen for ketamine based on route and indication for use
- Identify challenges regarding ketamine administration by non-physicians

Ketamine Mechanism of Action

- Dissociative anesthetic
- Structurally similar to phencyclidine (PCP)
- Unique because it provides sedation and analgesia
- Exerts sedative and analgesic action primarily through NMDA antagonism
- Also has affinity for opioid receptors

Ketamine Kinetics

- Onset of action
  - Intravenous: 45-60 seconds
  - Intramuscular: 3-5 minutes
- Duration of action
  - Intravenous: 5-15 minutes
  - Intramuscular: 30-45 minutes

Ketamine Contraindications

- Package insert states not to give in anyone whom a significant increase in blood pressure constitutes a serious hazard
- Absolute contraindications:
  - Acute chest pain
  - Acute global eye injury
  - Schizophrenia
  - Infants and children less than 3 months old
- Relative contraindications:
  - Procedures that will stimulate posterior pharynx
  - Consider not giving to patients with chronic cardiovascular disease such as heart failure, ischemic heart failure
  - Glaucoma

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Ketamine Side Effects

- Neurologic:
  - Dizziness, confusion, hallucinations, nystagmus, blurred vision
- Cardiovascular:
  - Hypotension and hypertension
  - Tachycardia and bradycardia
- Pulmonary:
  - Laryngospasm
- Gastrointestinal:
  - Nausea/vomiting
  - One study in pediatrics found reduced vomiting in patients given ondansetron before ketamine
  
Ann Emerg Med. 2008;52:30-34

Ketamine Dosing and Administration for Pain

- Primarily looked at for acute pain but can also be considered for chronic pain in patients who do not want opioids
- Idea is to give a sub-dissociative dose of ketamine
- Dose ranges from 0.1 to 0.3 mg/kg
  - Recommend a dose of 0.3 mg/kg
  - Suggest mixing dose in 50 mL of normal saline and administering over 20 minutes

Ketamine Literature for Pain

- Lots of studies ranging from ketamine vs. opioids to ketamine with opioids and need for rescue opioid therapy
- Overall literature suggests ketamine will decrease opioid use and in some situations can manage pain just as effectively as opioids alone
- Meta-analysis looking at literature published in 2016
- ACEP policy statement:
  - Safe to give using same procedures as opioids
  - Does not require intensive monitoring
  - List a wide variety of potential uses

http://www.acepnow.com/article/acep-policy-low-dose-ketamine/

Ketamine for Excited Delirium

- "Syndrome of uncertain etiology characterized by delirium, agitation, and hyperadrenergic autonomic dysfunction."
  - Stimulant abuse or other drugs account for majority of cases
  - Both salvia/synthetic cathinones include methylone, ethylone, and alpha-PVP (Flakka)
  - Mortality has been reported to be as high as 8%
    - Causes of death include hyperthermia and cardiovascular collapse
  - Ketamine has become a popular option due to its quick action and side effect profile
    - Does not lower seizure threshold
    - Does not impair heat dissipation


EMS Use of Ketamine

- Violent patients can be a danger to EMS staff just as much as the ER staff
- Patients can be difficult to restrain and keep restrained in moving vehicle
- EMS has less staff to restrain a patient
Pre-Hospital Ketamine for Delirium

- Midazolam along with all other benzodiazepines has a slower onset when given IM.
- Many EMS protocols give 10 mg of midazolam IM.
- Effective ketamine dose reported in literature ranges from 3-5 mg/kg IM.
- I recommend 4 mg/kg IM of total body weight and cap off at 500 mg.
- Doses less than 200 mg have been associated with treatment failure.
- Paramedics are allowed to give so long as the medical director has written a protocol allowing for its use.

Excited Delirium in the ER

- If no IV access has been established give 3-4 mg/kg IM.
- Many EMS protocols give 10 mg of midazolam IM.
- Effective ketamine dose reported in literature ranges from 3-5 mg/kg IM.
- I recommend 4 mg/kg IM of total body weight and cap off at 500 mg.
- Doses less than 200 mg have been associated with treatment failure.
- Paramedics are allowed to give so long as the medical director has written a protocol allowing for its use.

Florida Nursing Stance on Ketamine

- Florida nursing board view is based on intent.
- Ketamine is considered an anesthetic and can only be administered by a person credentialed in anesthesia.
- If intention is to produce an anesthetic state a registered nurse should not administer the medication.
- We do not allow ketamine to be given by a nurse for procedural sedation.

The Joint Commission Statement

“Individuals who are privileged to administer sedation must be able to rescue patients at whatever level of sedation or anesthesia is achieved either intentionally or unintentionally, e.g., when the patient slips from moderate into deep sedation or from deep sedation into full anesthesia.”

Cardiovascular Effects of Ketamine

- Ketamine both enhances and diminishes epinephrine induced arrhythmias.
- Can cause both bradycardia and tachycardia, hypertension and hypotension.
- Ketamine induced cardiac vasospasm can lead to severe hypertension and myocardial infarction or sudden cardiac death.
- We do not routinely recommend treating ketamine induced hypertension or tachycardia with anti-hypertensives.
- Treat ketamine induced hypertension and tachycardia with midazolam when feasible.

Ketamine for Procedural Sedation

- Ketamine 3-4 mg/kg IM
- Can be given into deltoid, buttocks, or thigh.
- Good idea to label the drawer in the automated machine for the 100 mg/mL concentration “IM use only” and adding a pop-up as well.
- Physicians are typically used to the 10 mg/mL concentration and may draw up the wrong volume in other indications without proper warnings.
- Can a nurse administer ketamine in this situation?
**Depth of Sedation**

- **Minimal Sedation** (Anxiolysis) is a drug-induced state during which patients respond normally to verbal commands.

- **Moderate Sedation/Analgesia** ("Conscious Sedation") is a drug-induced depression of consciousness during which patients respond purposefully to verbal commands, either alone or accompanied by light tactile stimulation.

- **Deep Sedation/Analgesia** is a drug-induced depression of consciousness during which patients cannot be easily aroused but respond purposefully following repeated or painful stimulation. The ability to independently maintain ventilatory function may be impaired.

**Making the Case for Ketamine**

- Ketamine is a favorable choice for procedural sedation for its respiratory safety profile.
- Allows for sedation and analgesia without suppressing the respiratory drive.
- Opioids should not be used during the case, can be given before or after.
- Few cases in literature of laryngospasm, or patients being intubated due to over sedation.
- Main concern is with emergence phenomenon.

**Emergence Phenomenon**

- While the medication is active patient is having delirium or dissociation due to confusion between imaginary and real stimuli.
- This reaction is not emergence phenomenon but is very common.
- Avoid this by telling patient to focus on happy thoughts.
- Administer with propofol (Ketofol).
- Give a benzo such as lorazepam or diazepam 30 minutes before procedure.
- Real emergence phenomenon happens after the medication effects subsides and patient has a momentary confusion from their dream state.
- Incidence in literature is less with pediatrics, but changes with age.
- Not recommend to pre-treat pediatric patients with benzodiazepines.

**Preventing bad Delirium**

- To avoid bad delirium do not administer ketamine alone.
  - Incidence is as high as 10-20% for monotherapy.
  - Prefer to give ketamine and propofol (Ketofol).
  - Give in separate syringes.
  - Administration order based on patient’s vitals.
  - Hypotensive patients start with ketamine, and hypertensive patients get propofol first.

**Dosing Ketamine for Procedural Sedation**

- Ketamine monotherapy 1 mg/kg IV.
  - Repeat doses of ketamine 0.5 mg/kg IV as needed.
- Ketamine with propofol 0.5-0.75 mg/kg IV.
  - Repeat doses of each at 0.5 mg/kg IV as needed.
  - Do not mix ketamine and propofol in same syringe.
  - Lose ability to administer the best agent based on patient’s vital signs.
  - Use the 10 mg/mL concentration of ketamine.

**Dealing with the Unexpected**

- If patients develop hypersalivation.
  - Try airway suctioning.
  - Nebulize ipratropium.
  - Last resort before intubation, try atropine 0.5 mg IV.
- Patients who develop laryngospasm will most likely end up intubated.
  - Happens so rarely we do not have a good idea of the incidence.
Safety First

- Ketamine for procedural sedation requires 2 physicians, one to perform the procedure and one to monitor the anesthesia
- Emergency Medicine residents are not credentialed in deep sedation and can only perform the procedure
- Recommend two consents one for the procedure and one for the sedation
- Capnography monitoring should be done on all patients requiring deep sedation
  - Used as a trending tool for patients who might be experiencing respiratory depression
  - Look at waveform for depth of breath and rate for hypoventilation

Waveform Capnography

- Normal Capnogram
- Normal EtCO₂: 35 – 45 mmHg

Ketamine for Rapid Sequence Intubation

- Ketamine dosing range is 1-2 mg/kg IV
  - Suggest giving 1.5-2 mg/kg IV
  - Giving 1 mg/kg for procedures and excited delirium, so we should give more for RSI
- Ketamine does cause bronchodilation
  - Dose that produces this effect is unknown
  - Good choice in status asthmatics cases
  - Ketamine has anti-epileptic properties can be a good choice in status epilepticus cases

Dosing and Advantage of Ketamine in RSI

Ketamine in High Intracranial Pressure Cases

- Ketamine thought to raise ICP by vasoconstriction, increase cerebral blood flow, and increasing cerebral oxygen consumption
- CPP=MAP-ICP
- Early studies show ketamine increases ICP
- Newer studies show ketamine is safe in patients with elevated ICP
- Consider using another agent unless patient is hypotensive

Sudden Cardiac Death with Ketamine

- Ketamine primarily increases blood pressure and heart rate through indirect stimulation of catecholamines
- Ketamine has negative inotropic effects
- Ketamine may cause severe hypotension and arrest in patients with impaired cardiac contractility along with diminished catecholamine states
- Should be extra careful with ketamine in cardiac disease when giving 2 mg/kg for RSI
  - Do not recommend lowering the dose to 0.5 mg/kg in shock states
Ketamine for Delayed Sequence Intubation (DSI)

- Hypoxia can cause delirium causing patients to rip off non-rebreather masks or Bi-PAP masks
- Administering ketamine can calm patients down while maintaining their respiratory drive so pre-oxygenation can occur without bag-mask ventilation
- Think of ketamine as procedural sedation where the procedure is pre-oxygenation
- Sometimes patients improve so well intubation can be avoided

References