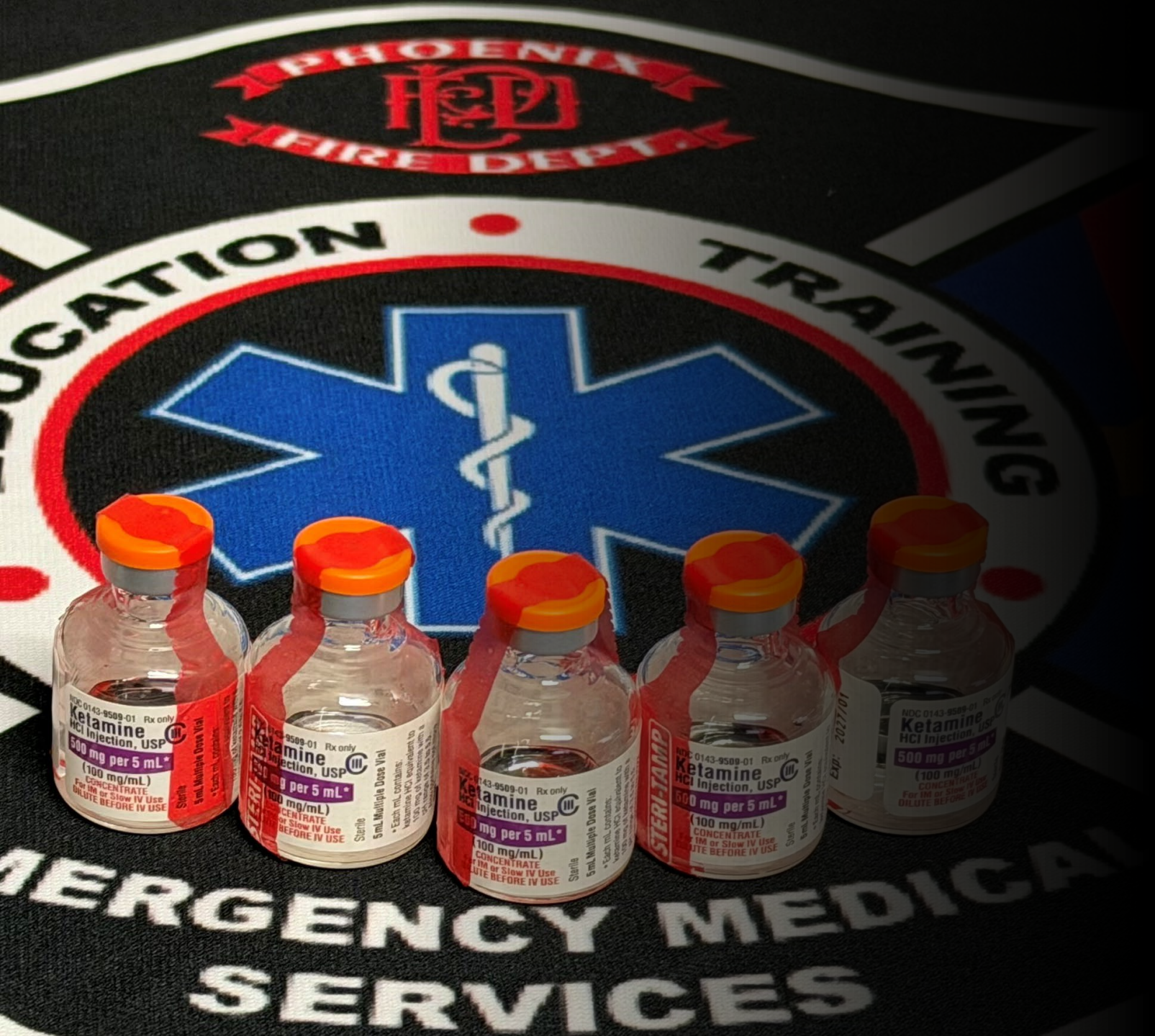


# AEMS
# EMS Odyssey

## Hyperactive Delirium: Ketamine Use in the Prehospital Setting

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Medical Director

Phoenix Fire Department


No Disclosures
PHOENIX
EST
1886
FIRE DEPT

# Objectives


| | |
|---|---|
| Define | Define hyperactive delirium |
| Discuss | Discuss EMS field management of agitated patients |
| Review | Review ketamine as an EMS-identified medication for patients with hyperactive delirium with agitation |
| Review | Review guidelines for hyperactive delirium with agitation |
| List | List contraindications for the use of ketamine in the EMS setting |
| Discuss | Discuss future expansion of ketamine use in the EMS setting |

# Online Medical Direction

Dispatched for a  Diabetic Problem


DELIRIUM
INABILITY
CONSCIOUSNESS
SYMPTOMATIC
DEMENTIA
NEUROPSYCHIATRIC
NEUROLEPTIC
RISK
BRAIN
UNDERLYING
DISTORTION
COMMON
DISORIENTATION
DELUSIONS
ALCOHOL
DECLINE
MENTAL
STATE
DYSFUNCTION
BENZODIAZEPINE
OLDER
ORGANIC
BASELINE
PERSON
TIME
DEMENTED
HALLUCINATION
COGNITIVE
HYPOACTIVE
UNMASKING
CAUSED
SYNDROME
TREMENS
PERSONS
SEVERE
MEDICAL
DISTURBANCE
COGNITION
SYMPTOM
MENTATION
DIAGNOSIS
INPATIENTS
PSYCHOSIS
PERCEPTUAL
FOCUS
PATIENT
DELIRIUM
ANTICHOLINERGICS
DISTINGUISH
DELIRIOUS
MISNOMERS
CONFUSION
DISORDER
ANTIPSYCHOTICS
ACUTE
ATTENTION
REORIENTATION
AGITATION


BIONICHEPHARMA
Ketamine Hydrochloride Injection, USP
500 mg/ 10 mL* (50 mg/mL)
Bioniche Pharma USA LLC, Lake Forest, IL 60045
Made in Ireland.
BIONICHEPHARMA
Ketamine Hydrochloride Injection, USP
1000 mg/ 10 mL* 100 mg/mL
Bioniche Pharma USA LLC, Lake Forest, IL 60045
Made in Ireland.
BIONICHEPHARMA
Ketamine Hydrochloride Injection, USP
200 mg/ 20 mL* (10 mg/mL)
Rx Only

# Hyperactive Delirium

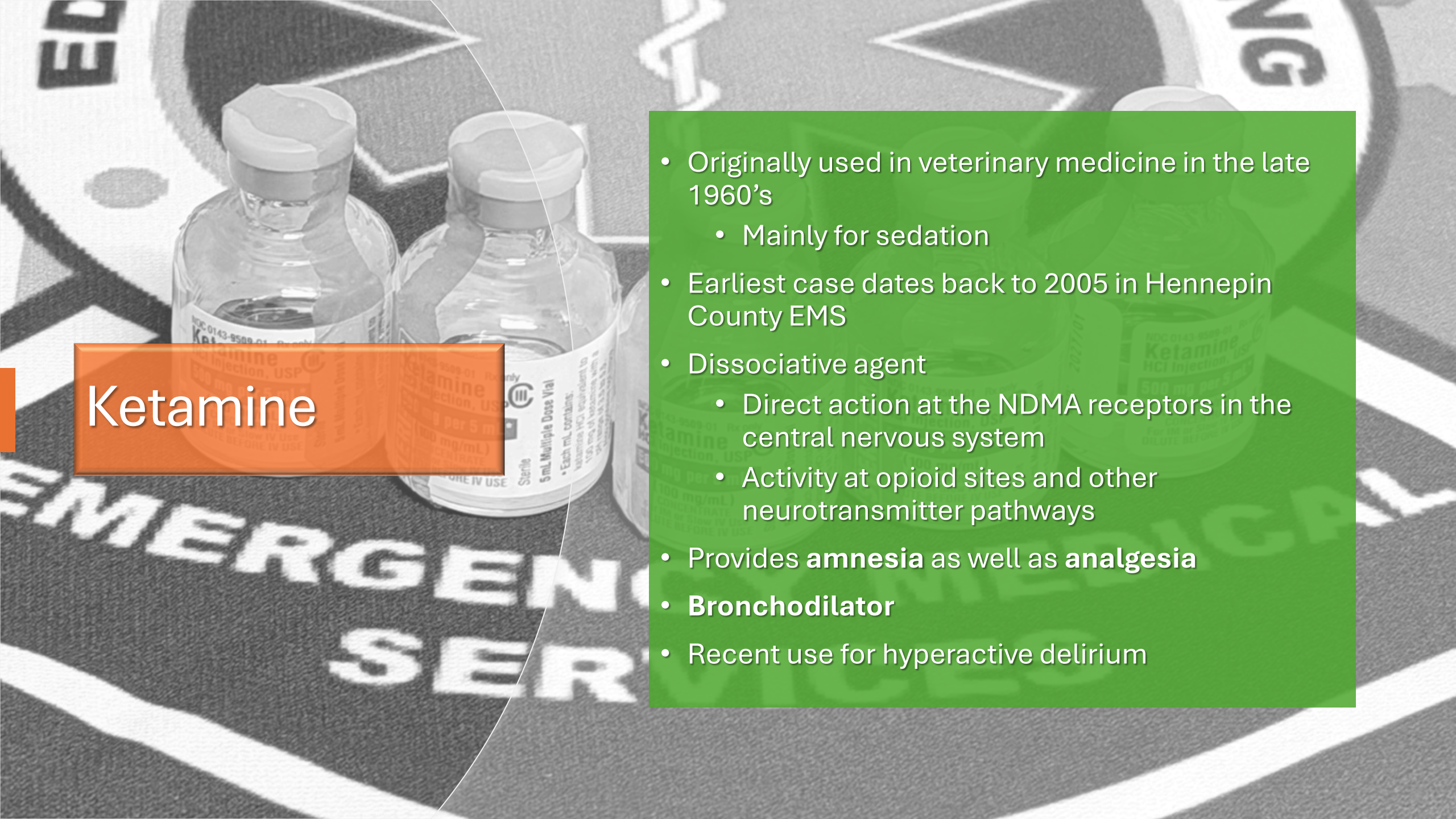
- A syndrome of uncertain etiology
- Characteristics:
  - **Delirium**
  - **Agitation**
  - **Hyperadrenergic autonomic dysfunction**
- Mortality (8%) resulting from hyperthermia, severe metabolic acidosis, and cardiovascular collapse
- High potential for patient to cause harm to first responders or endanger the public

# How do you control patients in the EMS setting who present wildly agitated?

- Patient and staff safety
- Intensive cooling
- Benzodiazepines (slower onset with IM dose)
- Antipsychotics (not in the EMS setting)
  - Concern for anticholinergic properties

If there were a medication that could be given as a single agent, in one dose, with a quick onset of action, and have minimal effects on respiratory drive.....


| | |
|---|---|
| A | Ativan |
| B | Midazolam |
| C | Fentanyl |
| D | Ketamine |



# Ketamine

- Originally used in veterinary medicine in the late 1960's
  - Mainly for sedation
- Earliest case dates back to 2005 in Hennepin County EMS
- Dissociative agent
  - Direct action at the NDMA receptors in the central nervous system
  - Activity at opioid sites and other neurotransmitter pathways
- Provides **amnesia** as well as **analgesia**
- **Bronchodilator**
- Recent use for hyperactive delirium

| | Ketamine | Fentanyl/midazolam | Haloperidol |
|---|---|---|---|
| Respiratory drive | Intact, preserved airway reflexes | Hypoventilation and apnea common | Intact, largely unaffected |
| Hemodynamics | Increased cardiac output; may have transient sinus tachycardia | Hypotension occurs especially in unstable patients | Hemodynamically neutral but potential for arrhythmia with qtc prolongation |
| Time of onset | 30 s IV, 3–4 min IM | 2–3 min IV, 10–15 min IM | 15–30 min IM, IV use discouraged by FDA |
| Effects | Analgesia, sedation, anxiolysis, amnesia | Fentanyl: analgesia, light sedation<br><br>Midazolam: anxiolysis, sedation, amnesia | Sedation, treatment of psychosis |

# Side effects

- Emergence Reactions – most likely
- Transient apnea when administered rapidly and in high doses
- Transient increase in heart rate and blood pressure
- Unclear with use in pregnancy and during breast feeding
- Laryngospasm is uncommon typically associated with large IM doses and overcome with positive pressure ventilation
- Nausea and Vomiting particularly when waking from sedation and is more pronounced in pediatric patients
- Increased intracranial pressure not shown to be factual

“And next let’s do a quick review of the research and science validating the out of hospital use of Ketamine.”

Kitch BB. *Out-of-hospital ketamine: review of a growing trend in patient care.* J Am Coll Emerg Physicians Open. 2020 Mar 10;1(3):183-189.

Ketamine is a unique medication with a long history of use in the emergency department. Out-of-hospital indications for ketamine have been explored and are currently expanding in some systems. This article supports use in the EMS setting due to favorable benefits with limited side effect profile.

Out-of-hospital indications for ketamine include airway management, rapid sequence induction, analgesia, sedation, and treatment of *excited delirium*.

# Burnett AM, et al. *Prehosp Emerg Care* 2012;16(4):553-9

In a quality improvement study, **13 patients** were administered IM ketamine for chemical restraint in the prehospital setting. Patients received **IM ketamine 5 mg/kg**. Very quick onset (~2 minutes) and produced moderate-to-deep sedation. 3 patients developed hypoxia (2 required intubation upon ED arrival). 5 of the 11 nonintubated patients required additional sedation and 3 patients experienced emergence reactions (which were successfully treated with midazolam and reassurance). It is unclear how much ketamine contributed to the hypoxia cases

# Iwanicki JL, et al. *Clin Toxicol* 2014;52:685-6. Abstract #9

35 patients who received IM ketamine **5 mg/kg** for excited delirium. Less than 1/3 required additional sedation. **Intubation rate decreased** over time as providers gained comfort in managing patients post ketamine administration. No cases of laryngospasm, emergency phenomena, or death were reported

What is the most appropriate dose to administer which helps maintain airway, cause less respiratory depression, while managing the agitated state?


| | |
|---|---|
| A | 1 mg/kg IM |
| B | 2-4 mg/kg IM |
| C | 2-4 mg/kg IV |
| D | 0.5 mg/kg IV |

Lin J, Figuerado Y, Montgomery A, Lee J, Cannis M, Norton VC, Calvo R, Sikand H. **Efficacy of ketamine for initial control of acute agitation in the emergency department: A randomized study.** Am J Emerg Med. 2021 Jun;44:306-311. doi: 10.1016/j.ajem.2020.04.013. PMID: 32340820

- 93 patients with excited delirium
- Ketamine vs Haldol/Benzo (IV/IM)
  - Dose:
    - Ketamine 4mg/kg IM (1mg/kg IV)
    - Haldol 10mg IM or IV/Ativan 2mg IM or IV
- Ketamine showed **quicker time to adequate sedation**, short-lived hypoxia, and no deaths (one death with Haldol/Ativan)
- Still needs evidence to support clinical patient selection

Borreani B, et al. *Ketamine for rapid control of hyperactive delirium with severe agitation. A retrospective comparison study.* JEM Reports, Vol 4, Issue 1, 2025, 100138

- Identified 66 patients with severe psychomotor agitation
  - Group 1 – 22 sedated with ketamine (5 mg/kg IM or 1 mg/kg IV) with droperidol (5 mg IM)
  - Group 2 – 22 sedated with ketamine (5 mg/kg IM or 1 mg/kg IV) alone
  - Group 3 – 22 sedated with midazolam (0.4 mg/kg IN or 0.1 mg/kg IV) with haloperidol 10 mg
- Patients treated with ketamine exhibit a significantly faster response, with immediate patient control, with greater safety than patients treated with midazolam.
- The combination of ketamine and droperidol increases clinical efficacy compared with ketamine alone
  - Patients treated with ketamine alone have resumption of agitation at the 30-minute mark

# What does all this mean….

We know IM ketamine works rapidly to produce sedation in hyperactive delirium

What is the optimal dose based on existing data?

Is there patients where we should not be using ketamine?

# Agitated, Combative, or Violent Patient/Behavioral Emergency: Adult & Pediatric



**Includes**: patients who are exhibiting agitated, violent, or uncooperative behavior or who are a danger to self or others.

Address underlying medical conditions may result in agitated or violent behavior. This includes but is not limited to:

- Traumatic Brain Injury (EPIC-TBI).
- Hypoglycemia, hypoxia.
- Postictal state, Seizures.
- Hyperthermia.
- Acute drug intoxication or withdrawal.

## EMT

- Dispatch law enforcement immediately when necessary to secure and maintain scene safety. Do not attempt to enter scene before safety is ensured.
- Initiate Universal Care.
- Provide supplemental oxygen as indicated.
- Obtain blood glucose level as soon as possible.
- Attempt verbal reassurance and calm patient.
- Engage family members/loved ones to encourage patient cooperation if their presence does not exacerbate the patient's agitation.

- Consider physical restraints, refer to Guidelines for Use of Restraints:
  Body:
  - Sheets can be used in addition to stretcher straps; place around the lower lumbar region, below buttocks, or around the thighs, knees and legs.
  - Do not apply restraints that restrict the patient's chest wall motion.

  Extremities:
  - Soft or leather restraints should not require key.
  - Restrain all four extremities to stationary frame of stretcher.

- Place stretcher in sitting position.
- If the patient is in police custody and in handcuffs a law enforcement officer must accompany the patient in the ambulance.

## Paramedic

- Apply cardiac monitor as soon as possible, particularly when pharmacologic management has been administered.
- Utilize $EtCO_2$ for all patients receiving pharmacologic management.
- Pharmacologic management should be based upon patient's clinical condition; use caution as all these medications can cause respiratory depression/compromise.
- Consider half dose in patients > 65 years old or with concern for co-ingestion with CNS depressant (EtOH, narcotics, etc.).
- Benzodiazepines:
  - Midazolam: 5 mg IM/IN/IV/IO. May repeat every 3 minutes. Max total dose 20 mg.
    or
  - Lorazepam: 2 mg IM or 2 mg IV/IO. May repeat once after 15 minutes, max total dose 4 mg.
    or
- Ketamine (Not indicated for postictal patients):
  - 4 mg/kg IM/IN, max 250 mg per administration. May repeat once after 5 minutes.

- Pharmacologic management should be a later consideration for pediatric patients.
- Benzodiazepines:
  - Midazolam:
  - 0.1 mg/kg IM or
  - 0.05 mg/kg IV/IO or
  - 0.3 mg/kg IN
  - Max dose 5 mg regardless of route
    or
  - Lorazepam:
  - 0.05 mg/kg IM/IV/IO.
  - Max dose 2 mg IM/IV/IO

- Ketamine is not indicated in pediatric patients.



| Adult Treatment Guideline Agitated, Combative Or Violent Patient/Behavioral Emergency | Phoenix Fire Department |
|---|---|
| **Includes:** Patients who are exhibiting agitated, violent, uncooperative behavior, or persons who are a danger to self, EMS crew, and/or bystanders.<br><br>Address underlying medical conditions that may result in agitated or violent behavior. This includes but is not limited to: Traumatic Brain Injury (EPIC-TBI), hypoglycemia, hypoxia, postictal state, seizures, hyperthermia, acute drug intoxication or withdrawal.<br><br>**High Risk Refusal:** Any patient that receives medication during initial treatment that alter the decision making capacity are considered a **High Risk Refusal and requires OLMD.** | **ATG 4-9** |

**Dispatch law enforcement when necessary to secure and maintain scene safety.**
Do not attempt to enter scene before safety is ensured.
Consider physical restraints to allow for patient care.
Patients in handcuffs must be accompanied by the appropriate law enforcement agency.

**Initiate Universal Care**

↓

Establish a patent airway.
Oxygenate and ventilate to maintain $SpO_2 \geq 94\%$.
Initiate ETCO2 monitoring.

↓

Obtain 4-lead ECG and consider obtaining 12-lead ECG.
Obtain IV/IO access if possible.
Administer 10 mL/kg LR/NS fluid bolus as indicated, may repeat once.
If blood glucose is ≤ 60 mg/dl, refer to ATG 4-3 Hypoglycemia

↓

**Consider sedation of patient for patient and crew safety;**

Ketamine **(Not indicated for postictal patients).**
1-2 mg/kg IV/IO push slowly over 1 min, **OR** 2-4 mg/kg IM.
Max 250 mg per dose. May repeat as indicated in 5 mins.
Max of 2 total doses.

**OR**

Midazolam 5-10 mg IM **OR** 2.5-5 mg IV/IO push slowly over 2 mins.
May repeat as indicated every 5 mins. Max total dose 20 mg.

**Observe for adverse effects and treat accordingly. Contact OLMD if additional medication is needed.**

***Caution: These medications can cause respiratory depression/compromise.* If ≥ 65 years or with concern for co-ingestion with CNS depression (EtOH, narcotics, etc.), consider giving half the calculated dose. *Constant monitoring of ABC's, vital signs, SpO2, and ETCO2 are necessary. Treat Appropriately.***

| Paramedic | |
|---|---|
| • Apply cardiac monitor as soon as possible, particularly when pharmacologic management has been administered.<br>• Utilize $EtCO_2$ for all patients receiving pharmacologic management.<br>• Pharmacologic management should be based upon patient's clinical condition; use caution as all these medications can cause respiratory depression/compromise.<br>• Consider half dose in patients > 65 years old or with concern for co-ingestion with CNS depressant (EtOH, narcotics, etc.).<br>• Benzodiazepines:<br>– **Midazolam:** 5 mg IM/IN/IV/IO. May repeat every 3 minutes. Max total dose 20 mg.<br>or<br>– **Lorazepam:** 2 mg IM or 2 mg IV/IO. May repeat once after 15 minutes, max total dose 4 mg.<br>or<br>• **Ketamine (Not indicated for postictal patients):**<br>– 4 mg/kg IM/IN, max 250 mg per administration. May repeat once after 5 minutes. | • Pharmacologic management should be a later consideration for pediatric patients.<br>• Benzodiazepines:<br>– **Midazolam;**<br>– 0.1 mg/kg IM or<br>– 0.05 mg/kg IV/IO or<br>– 0.3 mg/kg IN<br>– Max dose 5 mg regardless of route<br>or<br>– **Lorazepam:**<br>– 0.05 mg/kg IM/IV/IO.<br>– Max dose 2 mg IM/IV/IO<br><br>• Ketamine is not indicated in pediatric patients.<br>  |

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***Caution: These medications can cause respiratory depression/compromise.*** **If ≥ 65 years or with concern for co-ingestion with CNS depression (EtOH, narcotics, etc.), consider giving half the calculated dose.** ***Constant monitoring of ABC's, vital signs, SpO2, and ETCO2 are necessary. Treat Appropriately.***

# Final Thoughts

- Unique and versatile medication given:
  - Patient selection
  - Proper dose
  - Airway and Cardiac Monitoring
- Historical concern for increased ICP not based on evidence
- Emergence reactions rapidly managed with benzo’s
- Safe and effective for controlling the severely agitated patient
- Well within the out-of-hospital scope of practice and used to aid in providing safe and high-quality patient care

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