Emergency Medical Practice Advisory Council (EMPAC) - Ketamine Waiver Guidance

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Section 1: Ketamine (Ketalar) for Excited Delirium

In the spring of 2013, the Emergency Medical Practice Advisory Council (EMPAC) granted the first set of waivers allowing the use of ketamine to treat patients with a presumptive diagnosis of excited delirium in the field. The intent was to protect both patients and providers from the harm that can come from patients experiencing extreme agitation. Since the initial waivers were granted, a significant number of medical directors across the state have applied for ketamine waivers and ketamine is now one of the most frequently applied for ALS waivers in the state. Because of the large number of waiver applications for ketamine, the EMPAC determined that it was necessary to draft a guidance document, giving clear direction to both medical directors and the EMPAC, in order to ensure standardization and consistency in the process. This document is intended solely as guidance for medical directors as they develop protocols for ketamine use in the management of excited delirium and/or patients with extreme or profound agitation posing an immediate threat to the patient and/or providers. The guidelines or protocols developed by medical directors are expected to be specifically used by their agencies and this document, as a reference guideline, should not be considered the standard of care for management of excited delirium or agitation.

The use of ketamine for excited delirium and/or extreme or profound agitation is an emerging treatment indication; therefore it does not have a large body of evidence-based support in the literature. Across the country, many physicians question the existence of an excited delirium syndrome.

Management of agitation in the field is nothing new. The goal of agitation management is directed at providing the greatest amount of safety for patients and providers while using the most humane and respectful treatments. Agitation that is not thought to be due to an underlying medical or psychological etiology should be managed by police or other public safety providers. EMS providers should not engage in restraining people for law enforcement purposes.

The continuum of agitation

Agitation, like many conditions, has a continuum of severity. Mild agitation should be managed with verbal tools. Moderate to severe agitation should be managed with traditional sedatives including benzodiazepines and anti-psychotics. Extreme or profound agitation, which is uncommon, should be viewed as a behavioral emergency requiring prompt aggressive sedation to ensure patient and provider safety.

Excited Delirium Definition

Excited delirium is rare a medical emergency in which a person develops extreme agitation, aggressiveness, overheating, and exceptional strength that cannot be managed by routine physical or medical techniques. Excited delirium patients lose their mental capacity to stop resisting and are truly out of control. This type of extreme exertion may result in sudden death.

Treatment of Agitation

Treatment of agitation, even severe agitation, should be with benzodiazepines and/or antipsychotics.
Ketamine does not treat the underlying cause of excited delirium but addresses the behaviors exhibited by excited delirium. When necessary, ketamine may be used to treat behavior exhibited in extreme or profound agitation in order to rapidly facilitate patient care management and transport to the hospital.

**Indication for Treatment with Ketamine**

Prehospital providers should consider treatment for excited delirium and/or extreme or profound agitation with ketamine when a patient:

- Exhibits extreme or profound agitation placing themselves or providers in imminent danger
- Appears to lack the mental capacity to disengage from the struggle
- Has no option other than being restrained

**The Colorado Data**

Multiple agencies throughout the state have utilized ketamine for excited delirium and/or extreme or profound agitation. Denver Paramedics represents the majority of doses given for excited delirium or profound agitation. The EMPAC believes it is wise for interested medical directors to be aware of the most current reported data by CDPHE and Denver Paramedics from August 2017 to July 2018:

**CDPHE** had data for 291 patients who received ketamine for excited delirium or extreme or profound agitation (CDPHE data did not include Denver Paramedics in the August 2017 to July 2018 reporting year)
- Average age was 32 and 72% of patients were male
- Alcohol and drug use were the most common suspected causes of patient presentation
- Pre-hospital intubations occurred in 1% of cases
- Hospital intubations were reported in 18% of cases
- 6 patients with apnea
- 8 patients with hypersalivation

**Denver Paramedics** had 75,298 total transports with 136 patients who received ketamine
- 6,969 patients were restrained (9.3% of transports)
- 5,002 patients were sedated (6.6 of transports) with either midazolam (66%) or haloperidol (31%)
- 136 patients received ketamine for extreme agitation (0.18% of transports and 2.7% of sedated patients)
  - Of patients who received ketamine:
    - 6 pre-hospital intubations
    - In hospital follow up, there was around a **20%** intubation rate after transport to the facility
    - 8 patients with apnea
    - 12 patients with hyper-salivation
    - It appears that multiple sedatives prior to ketamine are associated with higher intubation rates.
    - Most patients who are intubated in the field or ED are admitted to the ICU

**Protocols for Agitation**

All EMS agencies should have a protocol that clearly defines the continuum of agitation and how to manage the care of patients falling anywhere on that continuum. Sample guidelines for the management of agitated patients in the field and for use of ketamine for suspected excited delirium and/or extreme or profound agitation are included at the end of this section.
Medical Oversight

Ketamine is a drug that has been shown to be effective for the treatment of excited delirium and/or extreme or profound agitation. However, it is also associated with a significant potential for complications and may lead to the need for intubation and admission to the Intensive Care Unit. Because of its potential safety concerns, ketamine is not within scope of practice for EMS providers below the level of Paramedic with Critical Care Endorsement as defined by Chapter Two Rules (6 CCR 1015-3 CHAPTER TWO - RULES PERTAINING TO EMS PRACTICE AND MEDICAL DIRECTOR OVERSIGHT). Outside of the P-CC scope, ketamine is only allowed by a special waiver, issued to EMS agency medical directors, when recommended by the EMPAC and approved by the Colorado Department of Public Health and Environment (CDPHE).

A successful ketamine waiver will demonstrate significant medical oversight by the EMS agency medical director receiving the waiver over the EMS providers to whom the medical director extends this practice. Included in this medical oversight is ongoing review of all cases by the medical director and reporting of data to the EMPAC. The EMPAC recommends that the medical director record and report the following data using the state reporting form for all patients treated with ketamine in the field for excited delirium and/or extreme or profound agitation:

- Demographics - age, gender, estimated weight
- Compliance with protocol
- Indication for use
- Vital signs (as soon as it is reasonable to obtain): BP, Heart rate, RR, EtC02, Sa02, and cardiac monitoring
- Suspected cause for excited delirium or extreme/profound agitation (Overdose, psychiatric, etc)
- Report all sedative medications and doses administered
- Documentation of airway/respiratory status and management
- Documentation of pre-hospital intubation or hospital intubation occurrence and reason for intubation
- Complications including apnea, respiratory depression, hyper-salivation, laryngospasm, bradycardia, cardiac arrest, hypotension, hypoxia, medication side effects, or other.
- Transport destination
- Patient disposition: D/C from ED, Admission to floor or ICU, Death
- Length of hospital stay
- If a death occurs, was the death related to the agitation, treatment, or other disease process
- Medical Director's documentation of review and appropriateness of use and treatment

Submission and Approval

Ketamine has multiple indications for which waivers have been previously approved including:

- A dissociative sedative for excited delirium and/or extreme or profound agitation
  - Indication of clear and present danger to patient, provider and/or public must exist prior to use
- Analgesia in pain management
- Induction in RSI (as part of any RSI Waiver)

Any completed waiver application submitted to the EMPAC will be reviewed and discussed by the council. The council will then make a recommendation to the department to either approve or deny the application. Additionally, applications may be withdrawn by the applicant or tabled by the council during the course of discussions. If an application is withdrawn or tabled, the medical director will be notified why the council felt they were unable to evaluate the waiver application well enough to make a
Ketamine waivers for excited delirium and/or extreme or profound agitation generally:

- Are approved for 3 years
- Are for patients 13 years of age and older
- Require annual reporting of data to the council for the calendar year (January 1 to December 31)
- Use IM dosing only
- Have a maximum of 5 mg/kg as a single dose prior to authorization from direct (online) medical control for additional doses
- Demonstrate robust medical oversight
- Require:
  - Continuous Sa02 monitoring
  - Continuous EtC02 monitoring
  - Continuous cardiac monitoring
- Note: In cases where ketamine is used for pain management in the backcountry environment and full patient care monitoring is not possible, constant patient engagement and pulse oximetry are minimal monitoring requirements for the use of ketamine

Summary

In order to provide the best possible care of EMS patients exhibiting agitation and to ensure the safety of EMS providers, the EMPAC recommends that medical directors provide their agencies with protocols that clearly define the appropriate treatment for patients who fall anywhere on the continuum of agitation and the tools necessary to accomplish those treatment guidelines. Each medical director is encouraged to equip their agency with the treatments and training most beneficial to their patients based upon where they fall on the agitation continuum and the needs and constraints of their local system. The EMPAC also recommends that ALS providers treat severe agitation appropriately, when indicated. Ketamine may be used for management of patients exhibiting such severe agitation that they are placing themselves and/or their providers in imminent danger. However, ketamine may be associated with high in-hospital intubation and ICU admission rates; therefore the use of ketamine should be approached with caution. Ketamine should not be used for patients who can be managed safely with traditional therapies.
**AGITATED/COMBATIVE PATIENT PROTOCOL**

**Patient is agitated and a danger to self or others**
- Attempt to reasonably address patient concerns
- Assemble personnel

Assume the patient has a medical cause of agitation and treat reversible causes

Does patient have signs of the Excited Delirium Syndrome?

No

Patient does not respond to verbal de-escalation techniques

Restraint Protocol
Obtain IV access as soon as may be safely accomplished

Still significantly agitated?

Sedate
- Consider cause of agitation
- Options: benzodiazepine or butyrophenone

Still significantly agitated?

- Repeat sedation dose
- If still significantly agitated 5 minutes after 2nd dose sedative, **Contact Base**

Consider Cause of Agitation:
Both benzodiazepines and butyrophenones (e.g. haloperidol) are acceptable options for agitated patients. In certain clinical scenarios individual medications may be preferred
- ETOH (butoyrophenone)
- Sympathomimetic (benzo)
- Psych (butoyrophenone)
- Head injury (butoyrophenone)

**Restraints**
No transport in hobble or prone position. Do not inhibit patient breathing, ventilations

Yes

**Excited Delirium Syndrome**
These patients are truly out of control and have a life-threatening medical emergency they will have some or all of the following sx:
- Paranoia, disorientation, hyper-aggression, hallucination, tachycardia, increased strength, hyperthermia

For adult patients with profound agitation that poses a risk to the patient and providers:
- Give **ketamine** 5 mg/kg IM
- Alternative: **midazolam** 5 mg IM

Patient Restraint Protocol

- Reassess ABCs post sedation
- High flow O₂
- Monitor for laryngospasm
- If needed, provide suction and BVM for respiratory support
- Start 2 large bore IVs as soon as may be safely accomplished
- Administer 2 liters NS bolus

- Full cardiac, SpO₂, EtCO₂ monitoring and rapid transport
- Start external cooling measures

**General Guideline:**
Emphasis should be placed on scene safety, appropriate use of restraints and aggressive treatment of the patient’s agitation.

**EMT**
**AEMT**
**EMT-I**
**Paramedic**
**KETAMINE**

**Description**
Ketamine is a non-competitive NMDA receptor antagonist and dissociative, amnestic, analgesic anesthetic agent.

**Onset & Duration**
- Onset: 1-5 minutes after IM administration.
- Duration: 10-15 minutes

**Indications**
Adult patient with signs of excited delirium where the safety of patient and/or providers is of substantial concern

**Contraindications**
- Relatively contraindicated in penetrating eye trauma
- Relative contraindication in patients with known cardiovascular disease (ketamine causes tachycardia)

**Side Effects**
- Laryngospasm: this very rare adverse reaction presents with strider and respiratory distress. After every administration of ketamine:
  - a. Prepare to provide respiratory support including bag-valve-mask ventilation and suction which are generally sufficient in rare cases of laryngospasm.
  - b. Institute cardiac monitoring, pulse oximetry and continuous waveform capnography
  - c. Establish IV or 10 access, check blood glucose
  - d. Establish and maintain physical restraint.
- Emergence reaction: presents as anxiety, agitation, apparent hallucinations or nightmares as ketamine is wearing off. For severe reactions, consider benzodiazepine.
- Nausea and Vomiting: always have suction available after ketamine administration. Give antiemetic as needed.
- Hypersalivation: Suction usually sufficient. If profound hypersalivation causing airway difficulty, administer atropine 0.5 mg IV.

**Dosage and Administration**
- **Adults:**
  - 5 mg/kg IM
  - Contact base for additional doses
- **Pediatric:**
  - Excited delirium is not reported in children and use of ketamine is not expected in pediatric patients

**Special Considerations**
- Excited delirium is a medical emergency. Expedite rapid and safe transport.
- Ketamine is provided for IM administration in 100 mg/ml concentration
- All cases of ketamine use will be reviewed by the Medical Director.

**ADDITIONAL INTERVENTIONS**
- Restraints
- Benzodiazepine
EMPAC Ketamine Waiver Guidance

Section 2: Ketamine (Ketalar) for Pain Management

Ketamine is a noncompetitive N-methyl D-aspartate (NOMA) receptor antagonist that blocks the release of glutamate, an excitatory neurotransmitter, but also binds to mu and kappa opioid receptors, thereby providing anesthesia, amnesia and analgesia. It is highly lipid soluble and thereby rapidly crosses the blood-brain barrier. It has a quick onset of action (peak concentration at 1 minute after IV push) and a short duration of action (5-15 minutes). At sub-dissociative doses (0.1 to 1.0 mg/ kg) ketamine provides analgesia while preserving airway patency, ventilation, and cardiovascular stability in most cases. When administered as an IV infusion as a slow drip, ketamine side effects and adverse reactions are significantly reduced. Ketamine also has bronchodilator effects.

Indications for Treatment with Ketamine

In EMS, ketamine has been proven to be safe and effective medication for pain management in Colorado. Ketamine has been typically utilized as an adjunctive medication to opioid therapy when standard methods of pain management are ineffective or allowed as a primary pain management medication in appropriate circumstances. The waiver application for the intended use would need to reflect the request.

The Colorado Data

Multiple agencies throughout the state have used ketamine as a therapeutic medication in pain management. The EMPAC believes it is wise for interested medical directors to be aware of the reported data by CDPHE from August 2017 to July 2018:

CDPHE had data for 976 patients who received ketamine (not including Denver Paramedics)
- Average age was 51 and 51.0% of patients were male
- Pre-hospital intubations occurred in 1 case
- Reporting of hospital intubations was not required and none were reported
- 7 patients with apnea
- 3 patients with hypotension
- 43 other side effects were reported including: altered mental status, musculoskeletal disturbances, and nausea/vomiting.

Medical Oversight

Ketamine is a drug that has been shown to be safe and effective adjunct to opioid therapy or when used as a single agent for treatment in pain management. Ketamine is currently not within scope of practice for EMS providers below the level of Paramedic with Critical Care Endorsement as defined by Chapter Two Rules (6 CCR 1015-3 CHAPTER TWO - RULES PERTAINING TO EMS PRACTICE AND MEDICAL DIRECTOR OVERSIGHT). Outside of the P-CC scope, ketamine is only allowed by a special waiver, issued to EMS agency medical directors, when recommended by the Emergency Medical Practice Advisory Council (EMPAC) and approved by the Colorado Department of Public Health and Environment (CDPHE).

A successful waiver for the use of Ketamine for analgesia in pain management will demonstrate significant medical oversight by the EMS agency medical director who receives the waiver over the EMS providers to
whom the medical director extends this practice. Included in this medical oversight is ongoing review of all cases by the medical director and reporting of data to the EMPAC. The EMPAC recommends that the medical director record and report the following data using the state reporting form for all patients treated with ketamine for pain management:

- Demographics - age, gender, estimated weight
- Compliance with protocol
- Administration route and doses given
- Documentation of vital signs - BP, Heart rate, RR, and continuous EtC02, SaO2, and cardiac monitoring.
- Additional medications given
- Any complications: apnea, respiratory depression, bradycardia, cardiac arrest, hypotension, hypoxia, laryngospasm, medication side effects, and other

**Submission and Approval**

Ketamine has multiple indications for which waivers have been previously approved including:

- A dissociative sedative for excited delirium
  - Indication of clear and present danger to patient, provider and/or public must exist prior to use
- Analgesia in pain management
- Induction in RSI (as part of any RSI Waiver)

A separate waiver is required for each of the above indications.

Any completed waiver application submitted to the EMPAC will be reviewed and discussed by the council. The council will then make a recommendation to the department to either approve or deny the application. Additionally, applications may be withdrawn by the applicant or tabled by the council during the course of discussions. If an application is withdrawn or tabled, the medical director will be notified why the council felt they were unable to evaluate the waiver application well enough to make a decision.

Ketamine waivers for pain management generally:

- Are approved for three years for patients of all ages
- Require annual reporting of data for the calendar year (January 1 to December 31)
- Are approved as an adjunct to opioid therapy but may also be used as a primary agent in appropriate circumstances
- Are approved for hemodynamically stable patients
- Have a maximum cumulative dose of 1 mg/kg IV/IO/IN/IM standing order prior to authorization from direct (online) medical control for additional doses
- Utilize an infusion drip administration for IV and IO routes
- Require:
  - Continuous SaO2 monitoring
  - Continuous EtC02 monitoring
  - Continuous cardiac monitoring
• Note: In cases where ketamine is used for pain management in the backcountry environment and full patient care monitoring is not possible, constant patient engagement and pulse oximetry are minimal monitoring requirements for the use of ketamine

Summary

Ketamine is a tool that can be used safely and effectively in pain management. However, due to its relative newness to both emergency medicine and emergency medical services, ketamine is currently not within scope of practice in Colorado and therefore currently requires a waiver for its use. It is through the tight medical oversight afforded by the waiver process that will allow for safety and efficacy of ketamine use in the field to be appropriately evaluated.
SAMPLE ANALGESIA GUIDELINE

Indications

Pain
Intubated patient

Assessment

Assessment should include, but not be limited to pain scale - overall impression of patient's comfort should be considered

Precautions / Contraindications

Apnea or hypoventilation (iatrogenic)
Caution should be used when combining multiple medications
Patient hypersensitivities to certain medications
Renal and hepatic impairment

Procedure

Non-invasive techniques, (e.g. calming, splinting and padding) may also be have some efficacy in analgesia
IV access
Consider Sp02, ETC02, or frequent conversation to guard against hypoventilation
Fentanyl should be considered first-line for any patient in pain, including cardiac
Opiates in combination with benzodiazepines may be considered for treatment of pain associated with spasms in orthopedic injury
  o Fentanyl and midazolam are the agents of choice due to rapid onset-of-action and short half life
  o Fentanyl should always be given first due to synergistic effects of the medications
  o Continuous monitoring of ETC02 must be used due to the increased concern for hypoventilation
Ketamine should be considered second-line in patients with long transport times; or instances where typical opiate strategy is not desired due to clinical, logistical or patient's concerns
  o Consider in pediatrics if no analgesia after two doses of fentanyl
Dilaudid is a third-line medication, most often used for interfacility transfers; or patients from the field where hospital admission is likely

Patients requiring pain management often have an indication for IV access. However, in cases where IV access is logistically or clinically unavailable, consider aerosolized administration.
**KETAMINE**

**Description**
Ketamine is a non-competitive NMDA receptor antagonist which produces complex neuroinhibition resulting in dissociative amnestic and analgesic effects.

**Onset & Duration**
- Onset: IV – Immediate, 1-5 minutes after IM administration.
- Duration: 10-15 minutes

**Indications**
- Adult patient with signs of excited delirium where the safety of patient and/or providers is of substantial concern
- Analgesia adjunct to opioid administration, intended to be second line therapy in situations where extreme pain has been unrelieved with appropriate opioid treatment.

**Contraindications**
- Relatively contraindicated in penetrating eye trauma

**Side Effects**
- Laryngospasm: this very rare adverse reaction presents with stridor and respiratory distress. After every administration of ketamine:
  a. Prepare to provide respiratory support including bag-valve-mask ventilation and suction which are generally sufficient in rare cases of laryngospasm.
  b. Institute cardiac monitoring, pulse oximetry and continuous waveform capnography
  c. Establish IV or IO access, check blood glucose
  d. Establish and maintain physical restraint.
- Emergence reaction: presents as anxiety, agitation, dysphoria, apparent hallucinations or nightmares as ketamine is wearing off. For severe reactions, consider benzodiazepine.
- Nausea and Vomiting: always have suction available after ketamine administration. Administer antiemetic as needed.
- Hypersalivation: Suction usually sufficient.
Dosage and Administration

**Excited Delirium**

**Adults:**
- 5 mg/kg IM
- Contact base for additional doses

**Pediatric:**
- Excited delirium is not reported in children and use of ketamine is not expected in pediatric patients

**Analgesia adjunct**

**Adults:**
- 0.25 mg/kg IV/IO single dose
- OR
  - 0.3 mg/kg IV/IO repeat PRN (likely every 20 minutes)
  - Dose for a typical adult female is 16 mg - 24 mg
  - Dose for a typical adult male is 24 mg - 40 mg
  - **Give dose in a 50 cc or more bag as a slow infusion to reduce psychotropic side effects and titrate to effect**
- 0.5 mg/kg IN/IM single dose
- OR
  - 0.5 mg/kg IN/IM repeat PRN (likely every 20 minutes)
  - Dose for a typical adult female is 30 mg - 40 mg
  - Dose for a typical adult male is 40 mg - 50 mg
  - Must make base contact after three doses
- Contact base for additional doses

**Pediatric:**
- 0.25 mg/kg IV/IO single dose
- OR
  - 0.3 mg/kg IV/IO repeat PRN (likely every 20 minutes)
  - Must make base contact after three doses
- 0.5 mg/kg IN/IM
- Contact base for additional doses

**Special Considerations**

- Excited delirium is a medical emergency. Expedite rapid and safe transport.
- Ketamine is provided for IM administration
- All cases of ketamine use will be reviewed by the Medical Director