

IM Ketamine for Acute Behavioral Agitation in VHA Emergency Departments and Urgent Care Centers

National Protocol Guidance

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VA Pharmacy Benefits Management Services, Medical Advisory Panel, VISN Pharmacist Executives, and the VHA National Emergency Medicine Office

Purpose: To provide general guidance on ensuring access to intramuscular (IM) ketamine for the treatment of acute agitation in VHA Emergency Department (ED) and Urgent Care Centers (UCC).

Disclaimer: To be consistent with the purpose of this general guidance and not to be overly prescriptive, this guidance allows facilities the flexibility to exercise modifications to the protocol as necessary to operationalize the use of IM ketamine for acute agitation.

Background

Ketamine is a glutamate N-methyl-D-aspartate (NMDA) receptor antagonist commonly used for general anesthesia, procedural sedation, pain management and treatment of acute behavioral agitation and major depressive disorder.

Acute behavioral agitation is a challenging problem in the emergency department given the risk of harm to patients and staff. Of note, there are no formal recommendations or standardization for the management of behavioral agitation. The administration of intramuscular sedatives in individuals with severe behavioral agitation is usually accomplished with benzodiazepines and/or antipsychotics². The use of benzodiazepines is associated with increased risk of respiratory depression, hypoxia, unplanned airway interventions and QTc prolongation². Ketamine is a noncompetitive N-methyl-D-aspartate receptor antagonist with dissociative effect at high doses and analgesia with lower doses³⁻⁸. Unlike benzodiazepines, ketamine has a rapid onset of action, favorable cardiovascular stability, preserves spontaneous respirations and protective airways reflexes⁸⁻¹¹. Studies have demonstrated that ketamine has quicker time to resolution of behavioral agitation when compared to other agents in both pre-hospital and hospital settings, making it an ideal agent for rapid treatment of acute behavioral agitation¹²⁻²⁰. Intramuscular ketamine may be particularly useful when treating individuals in whom establishing intravenous access is situationally challenging.

The American Society of Anesthesiologists and the American College of Emergency Physicians endorse that ketamine can be safely used in the emergency department and in prehospital care setting for the control of acute agitated delirium in psychotic emergencies and drug intoxications²¹.

This protocol does not apply to the use of ketamine for the purposes of deep sedation, acute pain management outside of sedation, when used for the purposes of securing an endotracheal airway (e.g., rapid sequence intubation), or when used in the care of mechanically ventilated patients.

Departments Affected: Pharmacy, Nursing, Emergency Departments/Urgent Care

Pharmacokinetics

- a. Onset – 5 minutes
- b. Duration – Up to 60 minutes
- c. Half-life – 2 to 3 hours

NOTE: IM ketamine may have significant variation in clinical effect between individuals, so caution is advised.

Patient Selection:

Inclusion Criteria

- Patients who are extremely combative and are at immediate risk of causing physical harm to medical staff, the public, or themselves
- Patients who have failed de-escalation techniques and one or more rapid tranquilization medications (e.g., benzodiazepines, droperidol, haloperidol, olanzapine, ziprasidone) or in whom ketamine is determined to be a preferred first line agent.

Indication

- a. Acute behavioral agitation (non-procedural sedation)

Contraindications

- a. Hypersensitivity to ketamine or any excipient

Precautions

- a. Active psychosis
- b. Pregnancy
- c. Elevated intracranial or intraocular pressure
- d. Severe cardiovascular disease: acute coronary syndrome, decompensated heart failure, severe valvular disease, active cardiac dysrhythmias
- e. Pulmonary hypertension
- f. Severe hepatic dysfunction

Dosing

- a. Intramuscular: 1-3 mg/kg (Ideal Body Weight)

NOTE: If ketamine is being administered shortly after receipt of another sedating agent, it is recommended to dose ketamine at the lower end of the dosing range.

Location of Administration, Monitoring , Equipment and Personnel Requirements

- Each facility will be responsible for developing and operationalizing a procedure to administer IM ketamine in the ED/UCC for the management of acute behavioral agitation.
 - The facility is responsible for monitoring the patient during and after the injection(s).
 - Be capable of administering oxygen, medication and/or restraints to manage potentially dangerous behavioral symptoms.
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- Bag Mask Valve (BVM) device and airway rescue equipment must be available immediately to the provider.
- The facility must have a plan to rapidly address any sustained alterations in cardiovascular function including advanced cardiac life support or transfer to a hospital capable of caring for acute cardiovascular events.
- A Licensed Independent Practitioner (LIP) with at least Out of Operating Room Airway Management (OORAM) Level 2 privileges must be available to be at the bedside immediately.
- The patient should be directly observed by an appropriate member of the clinical staff for at least 30 minutes after receiving IM ketamine.
- Non-invasive blood pressure monitoring, cardiac monitoring, continuous pulse oximetry and respiratory rate monitoring is recommended, as practical, in the environment of care.
- The ED/UCC LIP is responsible for ensuring that the patient is appropriate to receive ketamine for treatment of acute behavioral agitation, documenting risk and benefits and alternatives in the medical record.
- The ED/UCC RN is responsible for patient monitoring activities and may administer the medication under an appropriate order from an ED/UCC LIP consistent with applicable state licensure requirements.
- Facilities using ketamine for acute behavioral agitation will participate in an ongoing VA MedSAFE Medication Use Evaluation (MUE).

References

1. Wilkinson ST, Ballard ED, Bloch MH, et al. The effect of a single dose of intravenous ketamine on suicidal ideation: a systemic review and individual participant data meta- analysis. *Am J Psychiatry*. 2018;175(2):150-158.
2. Korczak V, Kirby A, Gunja N. Chemical agents for the sedation of agitated patients in the ED: a systematic review. *Am J Emerg Med*. 2016;34:2426-2431.
3. Sih K, Campbell SG, Tallon JM, et al. Ketamine in adult emergency medicine: controversies and recent advances. *Ann Pharmacother*.2011;45:1525-1534.
4. Motov S, Mai M, Pushkar I, et al. 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. *Am J Emerg Med*. 2017;35:1095-1100.
5. Andolfatto G, Willman E, Joo D, et al. Intranasal ketamine for analgesia in the emergency department: a prospective observational series. *Acad Emerg Med*. 2013;20:1050-1054.
6. Chudnofsky CR, Weber JE, Stoyanoff PJ, et al. A combination of midazolam and ketamine for procedural sedation and analgesia in adult emergency department patients. *Acad Emerg Med*. 2000;7:228-235.
7. Miner JR, Gray RO, Bahr J, et al. Randomized clinical trial of propofol versus ketamine for procedural sedation in the emergency department. *Acad Emerg Med*. 2010;17:604-611.
8. Andolfatto G, Abu-Laban RB, Zed PJ, et al. Ketamine-propofol combination (ketofol) versus propofol alone for emergency department procedural sedation and analgesia: a randomized double-blind trial. *Ann Emerg Med*. 2012;59:504-512; e1-2.
9. Green SM, Roback MG, Kennedy RM, et al. Clinical practice guideline for emergency department ketamine dissociative sedation: 2011 update. *Ann Emerg Med*. 2011;57:449-461.

10. Hosseinzadeh H, Eidy M, Golzari SE, et al. Hemodynamic stability during induction of anesthesia in elderly patients: propofol + ketamine versus propofol + etomidate. *J Cardiovasc Thorac Res.* 2013;5:51-54.
11. Ferguson I, Bell A, Treston G, et al. Propofol or ketofol for procedural sedation and analgesia in emergency medicine-the POKER study: a randomized double-blind clinical trial. *Ann Emerg Med.* 2016;68:574-582.e1.
12. Burnett AM, Peterson BK, Stellpflug SJ, et al. The association between ketamine given for prehospital chemical restraint with intubation and hospital admission. *Am J Emerg Med.* 2015;33:76-79.
13. Burnett AM, Salzman JG, Griffith KR, et al. The emergency department experience with prehospital ketamine: a case series of 13 patients. *Prehosp Emerg Care.* 2012;16:553-559.
14. Cole JB, Moore JC, Nystrom PC, et al. A prospective study of ketamine versus haloperidol for severe prehospital agitation. *Clin Toxicol (Phila).* 2016;54:556-562.
15. Cong ML, Humble I. A ketamine protocol and intubation rates for psychiatric air medical retrieval. *Air Med J.* 2015;34:357-359.
16. Le Cong M, Gynther B, Hunter E, et al. Ketamine sedation for patients with acute agitation and psychiatric illness requiring aeromedical retrieval. *Emerg Med J.* 2012;29:335-337.
17. Schepke KA, Braghiroli J, Shalaby M, et al. Prehospital use of IM ketamine for sedation of violent and agitated patients. *West J Emerg Med.* 2014;15:736-741.
18. Hopper AB, Vilke GM, Castillo EM, et al. Ketamine use for acute agitation in the emergency department. *J Emerg Med.* 2015;48:712-719.
19. Riddell J, Tran A, Bengiamin R, et al. Ketamine as a first-line treatment for severely agitated emergency department patients. *Am J Emerg Med.* 2017;35:1000-1004.
20. Barbic D, Andolfatto G, Grunau B et al. Rapid agitation control with ketamine in the emergency department: a blinded, randomized controlled trial. *Ann Emerg Med.* 2021;78:788-795.
21. American College of Emergency Physicians and American Society of Anesthesiologists Issue Joint Statement on Ketamine Use. August 26, 2020.
22. Morgan MM, Perina DG, Acquisto NM et al. Ketamine use in prehospital and hospital treatment of the acute trauma patient: a joint position statement. *Prehosp Emerg Care* 2021;25(4):588-592.
23. VHA Directive 1073(1). Moderate Sedation by Non-Anesthesia Providers. Amended January 13, 2023. Department of Veterans Affairs, Veterans Health Administration, Washington, D.C.