

REVIEW ARTICLE

Emergency Medical Services

Out-of-hospital ketamine: review of a growing trend in patient care

Bryan B. Kitch MD, FAEMS, FACEP 

Department of Emergency Medicine, East Carolina University, Greenville, North Carolina

Correspondence

Bryan B. Kitch, MD, Department of Emergency Medicine, East Carolina University, 600 Moye Blvd, 3ED, Greenville, NC 27834.
Email: kitchb@ecu.edu

Funding and support: By JACEP Open policy, all authors are required to disclose any and all commercial, financial, and other relationships in any way related to the subject of this article as per ICMJE conflict of interest guidelines (see www.icmje.org). The authors have stated that no such relationships exist.

Abstract

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 provides background on ketamine history and pharmacology, its use in the hospital environment and possible applications for emergency medical services usage of this medication. Contraindications and adverse reactions are discussed to provide education on the nuances of ketamine administration and mitigation strategies. Out-of-hospital indications for ketamine are discussed including airway management, rapid sequence induction, analgesia, sedation, and treatment of excited delirium.

KEYWORDS

EMS, medications, pharmacology, ketamine

1 | INTRODUCTION

Ketamine is a unique medication with decades of use in the medical field, originally used in veterinary medicine and for pediatric sedation.¹ First developed in the late 1960s and early 1970s, it has seen a recent upswing of interest due to its unique properties and multiple indications. Since the mid-2000s, and most recently in the past 5 years, increasing volumes of literature, resources, and clinical practice have involved this medication.¹⁵ Although primarily used in the emergency department and inpatient setting, the movement is growing for use of ketamine in the out-of-hospital setting.³ A review of this medication and summary of select relevant literature is useful for the field provider, medical directors, and emergency physicians who receive emergency medical services (EMS) patients.

Ketamine is classified as a dissociative agent. It has direct action primarily at the NMDA receptors in the central nervous system, but also has activity at opioid sites and other neurotransmitter pathways as well. The most similar compound to ketamine is the drug of abuse, phencyclidine.¹ Ketamine is classified as a schedule III controlled sub-

stance in the United States. When administered at sedation/anesthesia doses, the patient enters a dissociated state which is unlike other sedatives. The patient is often not unarousable as seen with medications like etomidate and propofol, but rather their consciousness is disconnected from their sensory input.⁴ Patients have been noted to speak or have occasional movement with this medication; however, they remain unaware of their surroundings. Patients will often have non-purposeful eye movements including various patterns of nystagmus.⁴ The unique patient response to this sedative requires provider experience to gain comfort, as the dissociative state can be unsettling. The effectiveness of ketamine comes from its ability to render a patient unresponsive to painful stimuli, while also providing amnesia to the procedure as well as analgesia.⁴

2 | EMERGENCY DEPARTMENT USE

As with many medications, the implementation of a out-of-hospital intervention such as ketamine is likely to mirror clinical practice inside

Supervising Editor: Alejandro Martin-Quiros, PhD.

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2020 The Authors. *JACEP Open* published by Wiley Periodicals, Inc. on behalf of the American College of Emergency Physicians.

TABLE 1 Comparison of ketamine versus fentanyl/midazolam versus haloperidol

	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 Midazolam: anxiolysis, sedation, amnesia	Sedation, treatment of psychosis
Dose for sedation	1–2 mg/kg IV, 4–5 mg/kg IM	Fentanyl: 0.5–1.5 mcg/kg IV every 1–2 min Midazolam: 1–2.5 mg IV over 2 min, repeat every 2 min until desired effect	5–10 mg IM
Drug–drug interactions	None proven; possible interaction with St. John's wort only.	Many, including increased risk of apnea with other sedatives and alcohol	Concern for torsades when given with other medications prolonging qtc; interactions with other dopamine modulators

the hospital. Ketamine is presently being used in many ED for a variety of indications.⁵ The pediatric emergency medicine community has had familiarity with this medication as an agent for procedural sedation where it is known to be well tolerated with limited side effects. Its use in pediatric patients is well studied in the literature and carries a Level A recommendation with regards to safety from the American College of Emergency Physicians (ACEP).⁵ Using ketamine for adult procedural sedation is gaining traction, although literature basis for safety is less well defined and carries a Level C recommendation for safety. The discussion on the use of ketamine for sedation purposes is largely driven by the reported risks and benefits of the drug, which will be discussed in detail.

Aside from procedural sedation and general anesthesia in the operating room, the two Food and Drug Administration (FDA)-labeled indications, other uses have been considered by some departments, and widely used by others. Rapid sequence induction for the purposes of airway management involves the use of a fast-acting sedative and a neuromuscular blocking agent. Ketamine has been used for the former indication as an ideal agent due to many of its physiologic properties. In the United States, drug shortages of etomidate in 2011 drove ED and EMS agencies to select a new medication that could induce unconsciousness without hypotension; ketamine was the agent of choice in many locations.⁶ Another use of this drug is for rapid sedation of the agitated patient. As it does during rapid sequence induction, ketamine produces rapid, reliable onset of unconsciousness with limited side effects, making it an ideal sedative for chemical restraint. Ketamine has also been shown to have bronchodilatory effects, and some consider it an adjunctive therapy for asthma exacerbation.⁷ Lower doses of ketamine than required for sedation are shown to have a role in analgesia.⁸ Last, interest is increasing in the use of ketamine for treatment of neuropsychiatric conditions such as migraine, chronic pain, and major depression.⁹

The recent surge in interest in the use of ketamine for a variety of conditions in the ED has led to a similar push for use and study in the out-of-hospital setting. Many of the current uses of ketamine in the hospital have begun in recent years and are not universally practiced throughout the emergency medicine community. Factors such as hospital protocols, credentialing/privileging of providers, training, and comfort levels all play a role with regards to in-hospital ketamine and influence the adoption of new indications.¹⁰

3 | REPORTED BENEFITS/RISKS

Many of ketamine's benefits are a reflection of its advantages over other medications. The reported side effects or adverse properties must also be discussed so that an informed choice can be made regarding medication selection. Specific properties of ketamine deserve further explanation in the following section; comparison to other methods of sedation can be found in the table (see Table 1).

3.1 | Airway, breathing, and circulation

One of the most important and clinically relevant effects of sedation/analgesia is the effect on respiratory drive and airway protection. Most all medications that can be used for sedation in rapid sequence induction induce apnea and loss of airway reflexes. Because ketamine works through an alternative pathway inducing dissociation rather than unconsciousness, the patient remains breathing on their own and able to protect their airway.¹¹ A large trial with over 800 patients noted that apnea with ketamine use is very rare and found that the airway and respiratory adverse events associated with ketamine was 3.9%. In this study risk factors that predicted ketamine-associated airway and

TABLE 2 Routes and dosing for ketamine

Route	Indication	Dose	Time of onset	Duration of action
Intranasal	Analgesia	1 mg/kg	2–3 min	Hours
IV—slow push/infusion	Analgesia	0.1–0.3 mg/kg	1–2 min	Hours
IV—slow push	Sedation/induction	1–2 mg/kg	1–2 min	10–20 min
Intramuscular	Sedation	4–5 mg/kg	4–7 min	20–30 min

respiratory adverse events were high intravenous doses, administration to children younger than 2 years or aged 13 years or older, and the use of co-administered anticholinergics or benzodiazepines.¹²

Some concern for increased salivation with ketamine exists; however, limited data exist to show a clinical impact, and traditional suction techniques have been effective in practice. Use of additional medications to manage secretions is generally not needed or advised.¹³ Ketamine's ability to allow for airway management without hypoxia has led some to consider its use for sedating a critically ill patient to pre-oxygenate prior to paralysis and intubation.¹⁴

Many medications used for sedation or analgesia can cause cardiovascular side effects. Common therapies such as intravenous morphine are well known to induce hypotension, often in a dose-dependent fashion. To the contrary, ketamine has sympathomimetic properties, increasing blood pressure and cardiac index.¹⁵ This makes ketamine an ideal agent for use in the hypotensive trauma or critically ill medical patient.⁶ Some concern exists that increasing cardiac output in patients with advanced cardiac disease is ill-advised; many providers avoid ketamine in this population; however, evidence is lacking regarding safety.¹⁶

4 | ADMINISTRATION

Ketamine proves itself to be a useful agent by its multiple routes of administration. Intravenous is the most rapid and predictable method to deliver the drug. Through the intravenous route, onset of action and recovery are most rapid and when given as a slow push over several minutes, adverse effects can be reduced.¹⁷ Intramuscular use is also easily used, with higher doses required than the intravenous route. It is considered safe and is well studied largely through its role in pediatric sedation, where obtaining intravenous access can be as difficult as the originally intended procedure. Safety is so well defined that ACEP guidelines on ED ketamine use do not mandate obtaining intravenous access during intramuscular ketamine sedation.¹⁸ The ability to achieve full dissociation through an intramuscular route has great implications for out-of-hospital management of conditions such as excited delirium and combative/intoxicated individuals. The intranasal route is also biologically favorable. Although literature is limited due to the ease of intramuscular use, intranasal ketamine has been used for analgesia with some success.¹⁹

Dosing varies depending on level of sedation needed. In 1 small adult out-of-hospital study ketamine dosing ranged 2.25–9.42 mg/kg intramuscular (mean, 5.26 mg/kg). Significant differences were noted between those who required intubation versus those who did not

(6.16 ± 1.62 mg/kg vs 4.90 ± 1.54 mg/kg).²⁰ Selection of the route of administration is largely dependent on patient factors. While the intravenous route allows for the most versatile and reliable drug response, intramuscular may be beneficial in children for whom the intravenous procedure is potentially traumatic, or in the combative patient where obtaining intravenous access is dangerous for staff. The intranasal route is best used for analgesia only in patients for whom the use of a needle is not preferred (see Table 2).

5 | EMERGENCE REACTIONS

Perhaps the most anecdotally cited concern regarding ketamine use in adults is that of the emergence reaction. Occasionally a patient waking up from ketamine dissociation can become agitated, confused and combative. Patients who suffer from this reaction are easily and best managed with benzodiazepine administration.¹⁸ Multiple studies have shown that benzodiazepines can be administered in escalating doses to rapidly and successfully reduce emergence effect, titrating based on patient response to therapy. Additionally, a benzodiazepine such as diazepam given prior to or alongside ketamine can potentially reduce emergence phenomenon.^{16,18} Patients with schizophrenia are considered at higher risk for this adverse effect. Many providers have reported that emergence reactions can be avoided by reducing stimuli such as commotion and loud noises, in addition to calming the patient prior to ketamine use.¹⁶

5.1 | Elevated intracranial pressure

One of the other concerns that had traditionally limited ketamine use to the healthy pediatric patient is the report of increasing intracranial pressure with administration. The greatest concern lies in the head injured or critical neurosurgical patient; increasing intracranial pressure with a medication in the setting of baseline pressure elevation could potentially be detrimental. Current guidelines and literature refute these concerns, as they are not evidence based. The initial fears of intracranial pressure elevation stem from case reports of patients with tumors and hydrocephalus from over 40 years ago.²¹

A systematic review in *Annals of Emergency Medicine* analyzed the available body of high quality evidence regarding intracranial pressure changes with ketamine use. Some studies showed scant increase in intracranial pressure while others actually showed a decrease. Blood flow to the brain (represented by cerebral perfusion pressure) was not changed. Even in patients having a slight intracranial pressure increase,

no adverse effect was reported on mortality, neurologic findings or length of stay in the ICU.²¹ Some have suggested that aside from patients with massive swelling in the ventricles of the brain (hydrocephalus), ketamine is completely safe to use with regards to intracranial pressure.²² ACEP considers intracranial pathology only a relative contraindication to ketamine use, not absolute.¹⁸

5.2 | Laryngospasm

Another risk of ketamine is laryngospasm, a closing of the vocal cords in the glottis leading to airway compromise. This complication is uncommon, occurring in less than third a percent of patients in a large compiled case series.¹² In such a rare event it is difficult to identify risk factors, but it seems associated with higher intramuscular doses of medication. Laryngospasm can at times be overcome by positive pressure mask ventilation (bag valve mask) or in severe cases with neuromuscular blockade. Airway positioning such as jaw-thrust and head-tilt may be beneficial in partial laryngospasm; however, if this is not successful, a complete spasm may be occurring and require positive pressure ventilation.²³ It should be noted that other commonly used sedative/induction agents such as etomidate and propofol both list laryngospasm as a possible adverse effect.

5.3 | Emesis

Ketamine has been known to cause nausea and vomiting, particularly when waking from sedation.²⁴ This is somewhat more pronounced in the pediatric population. Intramuscular use may have higher rates of emesis. Antiemetics, as typically used in EDs and EMS units, can be administered; vomiting is rarely severe.²⁵

6 | OUT-OF-HOSPITAL USE

The varying applications for ketamine in the inpatient and ED settings have had much study for the past decade and are rapidly becoming part of clinical practice. Many emergency medicine residency-trained physicians are gaining comfort with this medication for sedation. Out-of-hospital research is currently underway and several studies and reports have recently been published regarding EMS use of ketamine for several indications including:

6.1 | Airway management

In regions and services where rapid sequence induction is a commonly practiced skill, ketamine has rapidly gained traction as an induction agent prior to paralysis. Research has been published comparing ketamine for rapid sequence induction with usual therapies, often etomidate, and showed that ketamine has similar success and complication rates.⁶ Although out-of-hospital intubation is logistically much differ-

ent than ED intubation, pharmacologic properties are identical in both locations, and safety/efficacy data well established in the ED should logically translate to EMS. As a large number of patients receiving hospital rapid sequence induction are involved in trauma, the aforementioned data regarding lack of effect on intracranial pressure in head-injured patients should be considered as more evidence for the ability to safely use this drug. Additionally, the use of ketamine as an induction agent may cause resolution of the underlying pathology, allowing the skilled EMS provider to resuscitate a patient without paralytic use or endotracheal tube placement.¹⁴ This situation may occur when a patient is combative from hypoxia and unable to tolerate face-mask or other non-invasive ventilation. Dissociative dose ketamine as used for rapid sequence induction would calm the patient, allowing for appropriate oxygenation. The use of ketamine with a pause for oxygenation prior to paralysis and intubation may have benefit in reducing adverse effects associated with apnea and lead to improved clinical outcomes.¹⁴

6.2 | Chemical restraint

The EMS practitioner is one of the most likely medical providers to encounter acutely agitated, combative or dangerous patients who rapidly require care. These patients may be suffering from life-threatening injuries causing or coinciding with their mental status changes. The recently recognized excited delirium syndrome is a unique setting wherein the patient's agitation itself is life threatening. This critical illness often presents itself as a behavioral issue initially evaluated by law enforcement, timing of EMS involvement is variable and acuity is often high.²⁶ Rapid sedation and chemical (preferred over mechanical) restraint are essential to prevent morbidity and mortality. In all cases of acute behavioral/medical agitation, the EMS provider needs to be mindful of their own safety. They need to be able to rapidly administer a medication to control the patient without themselves being harmed. The medication needs to reliably sedate the patient and not induce additional harms such as hypoxia or seizures. Duration of action of the agent used should be long enough to allow initial assessment, interventions, and plans for further sedation/restraint. Ketamine is the ideal agent for chemical sedation, as it meets all the desired capabilities.²⁰ Although traditionally benzodiazepines have been used for sedation, dose response varies from patient to patient. Agitated patients may require higher than usual doses, sometimes exceeding offline protocol limits or even ambulance medication supply. Depending on co-ingestion, at high doses benzodiazepines can cause respiratory depression. Antipsychotics also have a role in sedating the combative patient but through the intramuscular route may have a longer than desired onset of action.²⁷ Haloperidol, a typical antipsychotic acting as a dopamine receptor antagonist, has been demonstrated to have some ability to provide out-of-hospital sedation of the agitated patient, with sedation occurring in about 25 minutes after 5 mg intramuscular administration.²⁸ When compared to 10 mg intramuscular haloperidol, ketamine 5 mg/kg intramuscular was able to provide much more rapid onset of sedation in the severely agitated patient. Sedation was

noted to occur at 5 minutes in the ketamine group and 17 minutes in the haloperidol group.²⁹

Several EMS services have created and implemented protocols to use ketamine for chemical restraint and treatment of excited delirium syndrome.^{27,30} As excited delirium represents a severe hypermetabolic state with a high mortality risk, rapid sedation to allow for cardiovascular support and resuscitation is essential to reduce mortality. Additionally, a patient suffering from excited delirium has high potential to cause harm to first responders or endanger the public requiring the use of lethal force.³¹ With its rapid onset and predictable complete dissociative anesthesia, ketamine seems to be an ideal agent for the treatment of excited delirium syndrome.^{27,30-31}

Recent literature published regarding ketamine for chemical restraint does reveal issues that need to be addressed or further studied for clarification. Unfortunately, as is often the case when only a few articles exist, a single report of laryngospasm in a patient has propagated through the body of evidence and frequently cited as a cause for concern.¹³ Carefully reviewing the initial report, the patient was well ventilated by bag valve mask and was electively intubated as a precaution, rather than an emergent intubation. Despite this 1 case that has been mentioned in multiple other papers, the rate of laryngospasm in large studies remains low and is referenced in the ACEP clinical policy on ketamine safe use.¹⁸

A report of ketamine use by the Columbus (Ohio) Division of Fire reported a clinical improvement of 91% of their agitated patients. This report also indicates that 23% of the patients were intubated either out-of-hospital or in the ED.³⁰ A separate study assessed this concern specifically and through analysis of a single center's data set, found a 29% intubation rate (all in the ED) of patients receiving intramuscular ketamine by EMS for restraint. The article notes that intubation rates of this level are not unique to ketamine and are common among EMS chemically restrained patients. Furthermore, the article cites that the main reason for intubation was "inability to protect the airway". This indication for intubation is highly subjective and was not further clarified from the emergency physician documentation. The receiving physician's familiarity with dissociative agents can easily play a role into the decision to intubate. Classic ED teaching of "Glasgow Coma Score (GCS) less than 8? Intubate!" for head trauma patients is often interpreted broadly, literally and dogmatically without consideration of confounding variables. A patient sedated with ketamine may well have a low GCS but be breathing and protecting their airway perfectly. If the ED care team is unaware that ketamine was administered, it would often be prudent to act quickly to manage the airway in a seemingly obtunded patient.

Patients requiring chemical restraint by EMS are high risk, high acuity patients regardless of intervention performed. Ketamine from a pharmacologic standpoint is the ideal agent; however, a mechanism to communicate with receiving staff of its use must be clearly defined. Ideally, physicians in the ED would have experience and comfort with this medication and its effects. Agencies currently using ketamine for agitation are encouraged to report their outcomes and protocols to increase the body of evidence and determine best safe practices for this indication.

6.3 | Analgesia

Pain is one of the most common reasons that patients present to EMS and ED. Treatment options available out-of-hospital are often limited by a variety of concerns, in addition to a lack of evidence supporting traditional therapies.³² Although a wide variety exists among EMS systems, a typical paramedic level unit will have 1 or 2 parenteral opioids, and at least 1 oral or non-opioid parenteral medication. Largely, acute severe pain is managed by opioid medications, as nonsteroidal anti-inflammatory drugs such as intravenous/intramuscular ketorolac provoke concerns of bleeding and renal injury. Opioids carry the well-documented risks of respiratory depression and hypotension. Barriers exist to effective out-of-hospital pain control, including limited doses in written protocols, need for online medical control, provider fears of being scolded for their use of medication, fear of "drug-seeking" patients, among many others.³³

Ketamine shows potential as a medication that can be used for safe and effective analgesia. The safety profile of ketamine used for sedation and induction is well established and discussed above. At much lower doses, ketamine can produce effective analgesia without dissociation. A systematic review analyzed the published out-of-hospital literature, finding 6 quality papers for analysis.³⁴ The majority of the contributing papers found that ketamine reduced additional analgesic needs or was just as efficacious as an opioid. Side effects were mild and airway complications were not observed. Another review article points out that specific studies regarding safety of out-of-hospital ketamine are very limited, but an identical paucity exists of evidence for current analgesia in use today. The authors of this study also conclude that the available evidence points towards safe and effective use of ketamine for analgesia by EMS as long as continued quality improvement and review of outcomes are performed.⁸ In a prehospital randomized control study, patients received either morphine or morphine plus ketamine for a long bone fracture. This study showed statistically significant decreases in morphine use and pain in the patients who received ketamine without any hemodynamic depression or adverse events.³⁵ A further margin of safety can be provided by ensuring the medication is given at a slow rate rather than a rapid intravenous push.³⁶ Low doses of ketamine have the potential to alleviate pain without significant side effects in the out-of-hospital population.

6.4 | Expanding out-of-hospital indications

As the medical community expands the use of ketamine to new indications in the hospital and clinic setting, some applications likely have future roles in the EMS environment.² The use of ketamine as an adjunctive agent for asthma management has growing potential and an increasing amount of research is being done to explore safety and efficacy.³⁷ Ketamine has some intrinsic properties as a bronchodilator and may be effective in improving the respiratory status during an asthma attack, either as an additional therapy or in place of other second and third line agents.³⁸ While traditional inhaled beta-agonists, steroids, and ventilation remain most important, the ease of which

ketamine can be administered may make it an ideal addition to the out-of-hospital formulary for this indication.³⁷ It has been suggested that ketamine may have a role in treating migraines and refractory headaches; however, randomized control trials have not been able to demonstrate the benefits seen in case reports.^{39,40} Ketamine has been mentioned as a possible treatment for depression and even suicidality.⁴¹ While the evidence is growing for this indication, the treatment requires further psychiatric evaluation, close monitoring, and results are not rapid enough in onset to fit the short out-of-hospital time frame.⁴² As further study of ketamine continues, some of the novel applications will likely become relevant to out-of-hospital care.

7 | CONCLUSIONS

Ketamine is a unique and versatile medication that is rapidly gaining popularity for a variety of emergency medical indications. Emergency physicians currently use ketamine for intubation, procedural sedation, analgesia, and chemical restraint. The efficacy of ketamine is proven, as is its safety. The historical concern of increased intracranial pressure was based on poor quality outdated reports and has been refuted by current evidence. Emergence reactions in adults are rapidly managed with benzodiazepines. Although little literature exists directly reporting EMS use, this medication could easily be implemented into out-of-hospital protocols. Ketamine offers a safe and effective method of controlling the severely agitated patient. EMS professionals, now a recognized medical subspecialty, must take the lead to educate the in-hospital emergency providers of the properties of this medication. It is a safe and effective medication for out-of-hospital sedation as long as the receiving ED staff is well educated on dissociative anesthesia and its management. Ketamine also can allow the out-of-hospital provider to augment analgesia in a safe and effective manner, reducing opioid requirements while decreasing suffering.

Continued research needs to be developed and published specific to EMS as our specialty reinforces itself with science and evidence. Additional direct studies of ketamine out-of-hospital use would definitely prove its place in the approved formulary. Regardless, the existing body of knowledge indicates use of ketamine is well within the out-of-hospital scope of practice and can be used to aid us all in providing safe and high quality patient care.

CONFLICT OF INTEREST

The author has no conflicts of interest to disclose. There was no external funding for this publication. Open access journal funds were paid for by the author and reimbursed from departmental reserve funds.

ORCID

Bryan B. Kitch MD, FAEMS, FACEP 
<https://orcid.org/0000-0002-6402-9000>

REFERENCES

- Mion G, Villevieille T. Ketamine pharmacology: an update (pharmacodynamics and molecular aspects, recent findings). *CNS Neurosci Ther*. 2013;19(6):370-380.
- Sheikh S, Hendry P. The expanding role of ketamine in the emergency department. *Drugs*. 2018;78(7):727-735.
- Jennings PA, Cameron P, Bernard S. Ketamine as an analgesic in the pre-hospital setting: a systematic review. *Acta Anaesthesiol Scand*. 2011;55(6):638-643.
- Zanos P, Moaddel R, Morris PJ, et al. Ketamine and ketamine metabolite pharmacology: insights into therapeutic mechanisms. *Pharmacol Rev*. 2018;70(3):621-660.
- Godwin SA, Burton JH, Gerardo CJ, et al. Clinical policy: procedural sedation and analgesia in the emergency department. *Ann Emerg Med*. 2014;63(2):247-258.e18.
- Price B, Arthur AO, Brunko M, Frantz P, Dickson JO, Judge T, Thomas SH. Hemodynamic consequences of ketamine vs etomidate for endotracheal intubation in the air medical setting. *Am J Emerg Med*. 2013;31(7):1124-1132.
- Jat KR, Chawla D. Ketamine for management of acute exacerbations of asthma in children. *Cochrane Database Syst Rev*. 2012;11:CD009293.
- Moy J, Le Clerc S. Ketamine in prehospital analgesia and anaesthesia. *Trends Anaesth Crit Care*. 2011;1(5-6):243-245.
- Murrough JW, Iosifescu DV, Chang LC, et al. Antidepressant efficacy of ketamine in treatment-resistant major depression: a two-site randomized controlled trial. *Am J Psychiatry*. 2013;170:1134-1142.
- Buckland DM, Crowe RP, Cash RE, et al. Ketamine in the prehospital environment: a national survey of paramedics in the United States. *Prehosp Disaster Med*. 2018;33(1):23-28.
- Kim G, Green SM, Denmark TK, Krauss B. Ventilatory response during dissociative sedation in children—a pilot study. *Acad Emerg Med*. 2003;10(2):140-145.
- Green SM, Roback MG, Krauss B, et al. Predictors of airway and respiratory adverse events with ketamine sedation in the emergency department: an individual-patient data meta-analysis of 8,282 children. *Ann Emerg Med*. 2009;54(2):158-168.e1-4.
- Burnett AM, Salzman JG, Griffith KR, Kroeger B, Frascione RJ. The emergency department experience with prehospital ketamine: a case series of 13 patients. *Prehosp Emerg Care*. 2012;16(4):553-559.
- Weingart SD. Preoxygenation, reoxygenation, and delayed sequence intubation in the emergency department. *J Emerg Med*. 2011;40(6):661-667.
- White PF, Way WL, Trevor AJ. Ketamine—its pharmacology and therapeutic uses. *Anesthesiology*. 1982;56(2):119-136.
- Green SM, Li J. Ketamine in adults: What emergency physicians need to know about patient selection and emergence reactions. *Acad Emerg Med*. 2000, Mar;7(3):278-281.
- Green SM, Rothrock SG, Harris T, Hopkins GA, Garrett W, Sherwin T. Intravenous ketamine for pediatric sedation in the emergency department: safety profile with 156 cases. *Acad Emerg Med*. 1998;5(10):971-976.
- Green SM, Roback MG, Kennedy RM, Krauss B. Clinical practice guideline for emergency department ketamine dissociative sedation: 2011 update. *Ann Emerg Med*. 2011;57(5):449-461.
- Johansson J, Sjöberg J, Nordgren M, Sandström E, Sjöberg F, Zetterström H. Prehospital analgesia using nasal administration of s-ketamine—a case series. *Scand J Trauma Resusc Emerg Med*. 2013; 21:38.
- 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(1):76-79.
- Cohen L, Athaide V, Wickham ME, Doyle-Waters MM, Rose NG, Hohl CM. The effect of ketamine on intracranial and cerebral perfusion pressure and health outcomes: a systematic review. *Ann Emerg Med*. 2015;65(1):43-51.e2.
- Green SM, Andolfatto G, Krauss BS. Ketamine and intracranial pressure: no contraindication except hydrocephalus. *Ann Emerg Med*. 2015;65(1):52-54.

23. Alalami AA, Ayoub CM, Baraka AS. Laryngospasm: review of different prevention and treatment modalities. *Paediatr Anaesth*. 2008;18(4):281-288.
24. Dunlop L, Hall D. BET 2: antiemetic use in paediatric sedation with ketamine. *Emerg Med J*. 2018;35(8):524-525.
25. Lee JS, Jeon WC, Park EJ, Min YG, Jung YS, Kim GW, Choi SC. Adjunctive atropine versus metoclopramide: Can we reduce ketamine-associated vomiting in young children? A prospective, randomized, open, controlled study. *Acad Emerg Med*. 2012;19(10):1128-1133.
26. Force AEDT. White paper report on excited delirium syndrome. American College of Emergency Physicians [Http://www. Ccpicd. Com/Documents/Excited% 20Delirium% 20Task% 20Force. Pdf](http://www.Ccpicd.Com/Documents/Excited%20Delirium%20Task%20Force.Pdf) (dernier Accès Le 21 Octobre 2013) 2009.
27. Ho JD, Smith SW, Nystrom PC, Dawes DM, Orozco BS, Cole JB, Heegaard WG. Successful management of excited delirium syndrome with prehospital ketamine: two case examples. *Prehosp Emerg Care*. 2013;17(2):274-279.
28. Isenberg DL, Jacobs D. Prehospital Agitation and Sedation Trial (PhAST): a randomized control trial of intramuscular haloperidol versus intramuscular midazolam for the sedation of the agitated or violent patient in the prehospital environment. *Prehosp Disaster Med*. 2015;30(5):491-495.
29. Cole JB, Moore JC, Nystrom PC, et al. A prospective study of ketamine versus haloperidol for severe prehospital agitation. *Clin Toxicol*. 2016;54(7):556-562.
30. Keseg D, Cortez E, Rund D, Caterino J. The use of prehospital ketamine for control of agitation in a metropolitan firefighter-based EMS system. *Prehosp Emerg Care*. 2015;19(1):110-115.
31. Scaggs TR, Glass DM, Hutchcraft MG, Weir WB. Prehospital ketamine is a safe and effective treatment for excited delirium in a community hospital based EMS System. *Prehosp Disaster Med*. 2016;31(5):563-569.
32. Borland ML, Jacobs I, Rogers IR. Options in prehospital analgesia. *Emerg Med*. 2002;14(1):77-84.
33. Thomas SH, Shewakramani S. Prehospital trauma analgesia. *J Emerg Med*. 2008;35(1):47-57.
34. Jennings PA, Cameron P, Bernard S. Ketamine as an analgesic in the pre-hospital setting: a systematic review. *Acta Anaesthesiol Scand*. 2011;55(6):638-643.
35. Johansson P, Kongstad P, Johansson A. The effect of combined treatment with morphine sulphate and low-dose ketamine in a prehospital setting. *Scand J Trauma Resusc Emerg Med*. 2009;17:61.
36. Henderson L. Ketamine considerations for prehospital use. *JEMS*. 2016;41(11). Available from: <https://www.jems.com/2016/10/31/ketamine-considerations-for-prehospital-use/>
37. Goyal S, Agrawal A. Ketamine in status asthmaticus: a review. *Indian J Crit Care Med*. 2013;17(3):154-161.
38. Tiwari A, Guglani V, Jat KR. Ketamine versus aminophylline for acute asthma in children: a randomized, controlled trial. *Ann Thorac Med*. 2016;11(4):283-288.
39. Benish T, Villalobos D, Love S, et al. The THINK (treatment of headache with intranasal ketamine) Trial: a randomized controlled trial comparing intranasal ketamine with intravenous metoclopramide. *J Emerg Med*. 2019;56(3):248-257.e1.
40. Etchison AR, Bos L, Ray M, et al. Low-dose ketamine does not improve migraine in the emergency department: a randomized placebo-controlled trial. *West J Emerg Med*. 2018;19(6):952-960.
41. Wilkinson ST, Ballard ED, Bloch MH, et al. The effect of a single dose of intravenous ketamine on suicidal ideation: a systematic review and individual participant data meta-analysis. *Am J Psychiatry*. 2018;175(2):150-158.
42. Fond G, Loundou A, Rabu C, et al. Ketamine administration in depressive disorders: a systematic review and meta-analysis. *Psychopharmacology*. 2014;231(18):3663-3676.

AUTHOR BIOGRAPHY



Bryan Kitch, MD is an Assistant Professor of Emergency Medicine at East Carolina University and the EMS medical director for Hyde County, NC, Martin County NC, the Eastern State Medical Assistance Disaster Team. Bryan is the assistant EMS medical director for Beaufort and Pitt Counties, NC. He is the medical advisor to the EMS education programs at Martin, Edgecombe, Wilson Community Colleges and the College of the Albermarle.

How to cite this article: Kitch BB. Out-of-hospital ketamine: review of a growing trend in patient care. *JACEP Open*. 2020;1:183-189. <https://doi.org/10.1002/emp2.12023>