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Subdissociative Ketamine Use in the Emergency Department

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ABSTRACT
Ketamine is an anesthetic known globally both for its potent dissociative properties and potential for abuse. More recently, ketamine demonstrates utility in a variety of disease states such as treatment-resistant depression, status asthmaticus, and acute agitation. In addition, ketamine has been shown to demonstrate various effects at different doses, which adds to its pharmacological benefit. As these new indications continue to come to light, it is important to stay current with the dosing for these indications as well as the adverse effects associated with ketamine's use. This review highlights the history and mechanism of ketamine as well as addressing the use of the different dosing ranges of ketamine. **Key words:** emergency department, ketamine, procedural sedation, subdissociative

KETAMINE is a medication with a complex and unique history that matches its pharmacological mechanism and indications for use. Since discovery in the 1960s, it has been used as an anesthetic, analgesic, sedative, and has been abused as a recreational hallucinogen. At present time, ketamine is being utilized with increasing frequency in the emergency department and in the intensive care unit. Literature is emerging regarding ketamine's increasing functionality in a variety of disease states, ranging from posttraumatic stress disorder to depression to status asthmaticus (Castle, Gray, Neehoff, & Glue, 2017; Cohen et al., 2015; Feder et al., 2014; Friedman, Soleimani, McGonigle, Egol, & Silverstein, 2014; Maher, Chen, & Mao, 2017; Newport et al., 2015). When this agent was first discovered, the adverse effects that were seen were poorly understood and as a result, ketamine's use was limited to emergent military situations and veterinary medicine (Domino, 2010). As the current understanding of ketamine improves and use of this agent expands, it is important to understand both the intentional and the unintentional effects in order to appropriately manage patients. This review discusses the off-label use of the lower dosage range of ketamine, referred to as subdissociative dose ketamine, as well as highlights the adverse effects and management of these complications.

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HISTORY

Ketamine (trade names include Ketalar, Ketaject, Ketaset, and Vetalar) was first originated in Detroit in the 1960s as a derivative of phencyclidine (PCP) (Domino, 2010). Phencyclidine was originally marketed as a potent amnestic with analgesic properties but was withdrawn from the market due to its adverse effects of postoperative confusion, hallucinations, and nonpurposeful movements. This dissociative property led to PCP's popularity and abuse as a substance of abuse (Hassan et al., 2017; Oovntan & Gool, 1970). With the withdrawal of PCP, the medical community began their search for an agent with similar amnestic and analgesic benefits without the adverse effects. Ketamine, then called CI-581, was designed as a derivative of PCP and became an attractive option for anesthesiologists after the studies showed the drug's unique ability to produce a marked degree of analgesia without a loss of consciousness. Unlike PCP, subjects did not experience the same degree of confusion and hallucinations. Literature at that time describes ketamine anesthesia dosing at doses of 1–2 mg/kg body weight intravenously, which would later be described as the dissociative dosing for this agent (Craven, 2007; Domino, 2010; Domino, Chodoff, & Corssen, 1965). Dissociation from ketamine was described as being aware and responsive without any response to painful stimuli (Domino et al., 1965). Doses lower than this would later become known as "subdissociative" (Castle et al., 2017; Domino et al., 1965; Maher et al., 2017; Oovntan & Gool, 1970). During the recovery period after ketamine administration, subjects were reported to have varying degrees of adverse reactions. Some patients remained entirely oriented whereas others showed changes in mood and demeanor; these changes varied by subject, with some displaying aggression and others becoming somnolent and withdrawn (Craven, 2007; Domino et al., 1965). Some subjects also reported hallucinations and confusion regarding what is real as they recovered from sedation with ketamine, although not to the extent of the reaction with PCP. This would become termed the "emergence phenomenon," later known as "ketamine dysphoria" (Aroke, Crawford, & Dungan, 2017).

MECHANISM

Glutamate is the main excitatory neurotransmitter in the central nervous system. One receptor that glutamate binds to for its excitatory effect in the brain is the *N*-methyl D-aspartate (NMDA) receptor (Newcomer, Farber, & Olney, 2000). Although the exact mechanism of ketamine is not well known, it is understood that ketamine binds to the NMDA receptors in the brain and prevents glutamate from activating these receptors. NMDA receptors affect many pathways in the brain involved in pain transmission and memory development, making them a target for treatment of many disease states. Ketamine binds to the NMDA receptor as a noncompetitive antagonist and exerts its effect independent of the amount of glutamate in the neuron synapse. Nitrous oxide is an NMDA antagonist that is administered as an inhaled amnestic and demonstrates anesthetic properties similar to ketamine. Tramadol and methadone have partial antagonist effects at the NMDA receptor and so help decrease pain via this mechanism independent of their opiate effects. Similarly, antagonism by ketamine at these receptors is expected to reduce excitatory transmission along pain pathways, producing analgesia and sedation (Kavalali & Monteggia, 2012).

Ketamine's properties seem to be dose dependent. As described in 1965, higher doses of ketamine will cause patients to experience a feeling of disconnection from their bodies, where patients will feel they are in a dream-like, out-of-body state. This is termed the dissociative dose, also known as high dose or anesthetic dose, and occurs at intravenous doses of 1–2 mg/kg of body weight or intramuscular at 3–6 mg/kg (Green, Roback, Kennedy, & Krauss, 2011; Hopper et al., 2015; Riddell, Tran, Bengiamin,

Hendey, & Armenian, 2017). Lower intravenous doses of 0.1–0.5 mg/kg of body weight or at intramuscular doses less than 3 mg/kg are described as subdissociative and do not cause this dissociation from self. It is this wide dosing range that provides its growing pharmacological benefit (Domino et al., 1965; Green et al., 2011; Lodge & Mercier, 2015). Unlike other anesthetics, ketamine offers maintenance of spontaneous respirations and protective airway reflexes, indicating that patients will usually not require intubation after administration (Aroke et al., 2017; Cromhout, 2003; Riddell et al., 2017). After one bolus of intravenous drug, ketamine demonstrates a brief half-life less than 15 min and a rapid elimination within 3 hr, although hepatic metabolism to the active metabolite, norketamine, may allow for the duration of ketamine's analgesic profile to be extended (Maher et al., 2017). Intravenous ketamine can have a duration of action for agitation as short as 15 min for one intravenous bolus and 30 min for a one-time intramuscular bolus, followed by a recovery period up to 3 hr after administration (Cromhout, 2003; Craven, 2007; Domino et al., 1965; Green et al., 2011). This results in a short duration of action of ketamine and often will require repeat dosing or intravenous continuous infusion to prolong the duration of action in the setting of dissociative ketamine dosing, although patients receiving subdissociative dosing will see extended time after administration in the recovery period (Craven, 2007; Cromhout, 2003; Long & Koyfman, 2018; Hopper et al., 2015). It is important to note that the duration of ketamine's action does depend on the indication, as patients receiving ketamine for suicidal ideation can see a duration as long as 2 weeks (Craven, 2007). Ketamine has oral bioavailability but is heavily metabolized by first-pass metabolism and so is more commonly administered via intravenous, intranasal, or intramuscular routes (Aroke et al., 2017; Reinstatler & Youssef, 2015). At low doses, ketamine is associated with relaxation and analgesia (Domino et al., 1965; Hassan et al., 2017), and when doses are increased to dissociative levels, the patients experience a dream-like state, which explains the appeal to recreational drug users (Hassan et al., 2017).

INDICATIONS FOR USE

In the emergency department setting, ketamine's use is growing rapidly in pediatric and adult populations. Literature is growing rapidly regarding the use of dissociative ketamine dosing in acutely agitated patients, both in the prehospital setting and once patients have arrived to the emergency department (Cole et al., 2016; Hopper et al., 2015; Melamed, Oron, Ben-Avraham, Blumenfeld, & Lin, 2007; Riddell et al., 2017). Dissociative dosing strategies are also utilized in the emergency department for procedural sedation (Cromhout, 2003; Green et al., 2011). Lower, subdissociative doses of ketamine are frequently utilized for a variety of reasons as well. In order to reduce unnecessary opiate utilization, administration of subdissociative ketamine has been shown to reduce or eliminate the amount of opiates a patient receives for analgesia (Craven, 2007; Gibbons, 2012; Honey et al., 2003, 2004; Sin et al., 2015). One example of the novel analgesic effect is the use of ketamine for treatment of headaches and migraines (Long & Koyfman, 2018). Patients with suicidal ideations, posttraumatic stress disorder, or treatment-refractory depression have successfully been bridged to antidepressant therapy with intravenous ketamine at these subdissociative doses (Cottrell & Hartung, 2016; Feder et al., 2014; Kavalali & Monteggia, 2012; Lodge & Mercier, 2015; Newport et al., 2015; Reinstatler & Youssef, 2015). Although ketamine has been used frequently in pediatric procedural sedation, it is now gaining popularity as a treatment for status asthmaticus in this patient population (Craven, 2007). As discussed previously, these dosing ranges optimize ketamine's subdissociative dosing strategies. For many of these subdissociative indications, intravenous administration is the best studied, although there are case reports growing regarding

intranasal and intramuscular administration for these indications as well. A summary of these dosing ranges and their indications are provided in Table 1.

Ketamine is supplied as racemic ketamine via three different concentrations of 10, 50, or 100 mg/ml (Craven, 2007). The higher concentration lends itself to more efficient administration via intramuscular route. The drug does not require dilution and can be administered over 1 minute per the manufacturing packing insert. Intravenous administration for indications such as status asthmaticus and suicidal ideation has been studied with dilutions in either normal saline or dextrose 5% solution and provided over a 40-min infusion time (Reinstatler & Youssef, 2015).

When evaluating a patient's appropriateness for ketamine, it is important to note the contraindications and precautions that limit its use. The increase in lacrimation, gastrointestinal secretions, and bronchorrhea seen with ketamine administration make aspiration a concern for some patients. For this reason, aspiration risk should be evaluated for each patient and appropriate precautions should be implemented as necessary (Craven, 2007; Cromhout, 2003; Domino, 2010). Because of its dissociative effects, ketamine has demonstrated an ability to exacerbate schizophrenia and should be avoided in this patient population (Hopper et al., 2015). Ketamine has been anecdotally observed to complicate the airway of infants younger than 3 months, although this may be secondary to physiological differences in the anatomy of this population and not specific to ketamine alone (Bhatt et al., 2017; Cromhout, 2003; Green et al., 2011).

ADVERSE EFFECTS

There are several adverse effects that are common with ketamine administration. Where

Table 1. Comparison of dosing strategies for ketamine usage

Dosing strategy	Indication	Dosing
Subdissociative	Suicidal ideation/ treatment-resistant depression	0.5 mg/kg iv two to three times per week (Singh et al., 2016)
		0.2–0.5 mg/kg iv (Hopper et al., 2015)
		1.5–3 mg/kg PO once monthly (Reinstatler & Youssef, 2015)
	Treatment-refractory anxiety	0.51 mg/kg iv (Castle et al., 2017)
	Opiate-sparing or adjunctive analgesia	0.1 mg/kg iv (Craven, 2007)
		0.2–0.5 mg/kg iv (Sin, Ternas, & Motov, 2015)
		50–100 mg PO three times daily
	Posttraumatic stress disorder	0.5 mg/kg iv (Feder et al., 2014)
	Status asthmaticus	0.2 mg/kg iv bolus with 0.5 mg/kg/hr for 3 hr iv continuous (Craven, 2007)
	Migraine	0.1–0.3 mg/kg iv (Long & Koyfman, 2018)
Dissociative	Acute agitation	1–2 mg/kg iv (Riddell et al., 2017)
		3–6 mg/kg im (Cole et al., 2016; Cromhout, 2003; Hopper et al., 2015; Riddell et al., 2017)
	Rapid sequence intubation	1–2 mg/kg iv bolus (Craven, 2007; Cromhout, 2003)
		3–5 mg/kg im (Craven, 2007)
	Procedural sedation	1–2 mg/kg iv bolus followed by 0.5 mg/kg maintenance incremental boluses (Craven, 2007; Green et al., 2011)

Note. im = intramuscular; iv = intravenous; PO = by mouth.

many sedative agents cause a decrease in blood pressure, ketamine is thought to cause dose-dependent stimulation of the central nervous system and prevent the reuptake of catecholamines, thereby associated with a theoretical sympathetic surge (Domino, 2010; Jakobsen et al., 2010). Because of this mechanism, ketamine has been shown to cause an increase in heart rate up to 25% of baseline as well as an increase in systolic blood pressure and cardiac output (Jakobsen et al., 2010). It has been speculated that this may make ketamine inappropriate for patients with ischemic heart disease because of increased demand on the heart, although this has not been well studied at doses commonly used today, and is often preferred compared with the hypotensive effects of other sedatives (Craven, 2007; Cromhout, 2003; Jakobsen et al., 2010). Other common adverse effects associated with ketamine include emesis and hypersalivation (Craven, 2007; Green et al., 2011). Providers trained in airway management should be available or supervise ketamine administration as either adverse effect may compromise the patient's airway. After administration of ketamine, patients can experience some movement disorders unrelated to painful stimuli, such as ataxia and hypertonicity (Green et al., 2011). These patients may require support with physical immobilization during procedural sedation (Craven, 2007; Green et al., 2011)

Less commonly, patients may experience respiratory depression, although recent literature describes this with fewer incidences as providers become comfortable with ketamine's use (Hopper et al., 2015). Laryngospasm is described in the pediatric population at an incidence of 0.3% and is thought to be caused secondary to stimulation of the posterior pharynx, as ketamine helps preserve the patient's natural protective airway reflexes (Green et al., 2011). It is speculated that the decreasing incidence of this adverse effect is due to both provider comfort with ketamine and lower dose strategies to prevent oversedation and dissociation (Craven, 2007; Green et al., 2011).

Emesis is documented at rates of 5%–15% and frequently occurs late in recovery when patients are awake and able to protect their airway. For this reason, prophylactic antiemetics should be evaluated as a risk-versus-benefit scenario and nursing staff should pay close attention to patients with a high aspiration risk (Craven, 2007; Green et al., 2011).

One of the unique challenges with ketamine use in the emergency department involves its hallucinatory reactions, as ketamine is metabolized and patients enter the recovery period, known as the emergence phenomenon. Literature describes this incidence at a very low rate of 1.4% when administered in the pediatric population, whereas the incidence in adults varies from 0% to 30% (Aroke et al., 2017; Craven, 2007; Green et al., 2011). When these hallucinations do occur, emergency medicine literature describes the reaction as mild, although patients can have recovery agitation without the presence of hallucinations. The frequency of the emergence phenomenon symptoms in adult patients is decreased in elderly patients and is associated with receipt of higher doses, and longer durations of ketamine therapy (Aroke et al., 2017; Craven, 2007). Symptoms of this adverse effect of ketamine closely resemble schizophrenia and increase a patient's risk of injury. Current therapy for the emergence phenomenon in the setting of ketamine administration involves a multimodal approach. Most typically, ketamine intravenous protocols will have the administration of a benzodiazepine such as lorazepam or midazolam as needed in the setting of acute psychosis (Aroke et al., 2017; Craven, 2007; Green et al., 2011). Some emergency department protocols will administer prophylactic benzodiazepines to prevent or reduce the incidence of the recovery reactions in adults, although the data supporting this intervention are lacking. However, sedatives should be readily available in case of severe agitation. In children, there does not seem to be a benefit to this prophylactic administration and so it is not recommended routinely

(Green et al., 2011). Other options described in the literature to address this adverse effect include clonidine or propofol administration as well as patient orientation. As discussed previously, orientation of the patient and maintenance of a low-stimuli environment can reduce the incidence of the emergence phenomenon. Anecdotal evidence suggests that patient orientation and recovery in a supervised location with reduced stimulation may reduce this incidence (Craven, 2007, Green et al., 2011).

PATIENT MONITORING AND EDUCATION

One benefit to administration of ketamine is the maintenance of hemodynamic stability in comparison to other anesthetics, making this an appealing agent in emergent situations with tenuous cardiovascular status (Cromhout, 2003; Green et al., 2011). Administration of ketamine can cause a dramatic increase in secretions in the lungs, mouth, and gastrointestinal system (Craven, 2007; Green et al., 2011). In order to prevent these more common effects, some hospital protocols will administer prophylactic anticholinergics for hypersecretions (Green et al., 2011). For treatment of hypersalivation, atropine or glycopyrrolate is often prophylactically or concomitantly given especially in patients at high risk of aspiration secondary to salivation, with choice of agent based on physician preference (Craven, 2007). Due to ketamine's effects on patient movement and coordination, current recommendations include ensuring purposeful neuromuscular activity prior to discharge (Green et al., 2011). Strategies to reduce the incidence of respiratory depression include provider and nursing education regarding the opiate-sparing effects of ketamine; the ability to reduce the dose of concomitant medications, which can cause respiratory depression, may help reduce this complication in the future. Table 2 is a summary of antidotal agents discussed here.

CONCLUSION

From novel anesthetic to recreational drug to antidepressant agent, ketamine's use over the decades has evolved as understanding of its mechanisms and adverse effects evolves. As further research continues into ketamine's use and management, it is important for practitioners to become familiar with all of ketamine's effects. In understanding ketamine's colorful history, practitioners can better utilize the drug to prevent and mitigate the adverse effects that were once poorly understood. It is through comfort in prescribing and administering ketamine with appropriate understanding of the challenges that patients can take benefit from new alternatives for treatments and emergency departments can offer novel, literature-based care for patients.

Table 2. Anecdotal agents described in literature for adverse effects of ketamine administration

Adverse effect	Agent	Dosing
Hypersalivation	Glycopyrrolate (Craven, 2007)	0.01 mg/kg iv with maximum dose 0.2 mg
	Atropine (Craven, 2007)	10–20 mcg/kg iv with maximum dose 0.5 mg
Emergence reaction	Benzodiazepines	
	Diazepam (Craven, 2007)	0.15 mg/kg PO 1 hr prior to induction 0.1 mg/kg iv alongside ketamine induction
	Midazolam (Green et al., 2011)	0.03 mg/kg iv
Emesis	Ondansetron (Green et al., 2011)	0.15 mg/kg iv with maximum dose 4 mg

Note. iv = intravenous; PO = by mouth.

REFERENCES

Aroke, E. N., Crawford, S. L., & Dungan, J. R. (2017). Pharmacogenetics of ketamine-induced emergence phenomena: A pilot study. *Nursing Research*, *66*(2), 105–114.

Bhatt, M., Johnson, D. W., Chan, J., Taljaard, M., Barrowman, N., Farion, K. J., . . . Sedation Safety Study Group of Pediatric Emergency Research Canada (PERC). (2017). Risk factors for adverse events in emergency department procedural sedation for children. *JAMA Pediatrics*, *171*(10), 957–964.

Castle, C., Gray, A., Neehoff, S., & Glue, P. (2017). Effect of ketamine dose on self-rated dissociation in patients with treatment refractory anxiety disorders. *Journal of Psychopharmacology*, *31*(10), 1306–1311.

Cohen, L., Athaide, V., Wickham, M. E., Doyle-Waters, M. M., Rose, N. G., & Hohl, C. M. (2015). The effect of ketamine on intracranial and cerebral perfusion pressure and health outcomes: A systematic review. *Annals of Emergency Medicine*, *65*(1), 43–51.e2.

Cole, J. B., Moore, J. C., Nystrom, P. C., Orozco, B. S., Stellpflug, S. J., Kornas, R. L., . . . Ho, J. D. (2016). A prospective study of ketamine versus haloperidol for severe prehospital agitation. *Clinical Toxicology (Philadelphia, PA)*, *54*(7), 556–562.

Cottrell, J. E., & Hartung, J. (2016). Ketamine versus special K: A double-edged sword. *Anesthesia & Analgesia*, *122*(3), 586.

Craven, R. (2007). Ketamine. *Anaesthesia*, *62*(Suppl. 1), 48–53.

Cromhout, A. (2003). Ketamine: Its use in the emergency department. *Emergency Medicine (Fremantle)*, *15*(2), 155–159.

Domino, E. F. (2010). Taming the ketamine tiger. 1965. *Anesthesiology*, *113*(3), 678–684.

Domino, E. F., Chodoff, P., & Corssen, G. (1965). Pharmacologic effects of Ci-581: A new dissociative anesthetic, in man. *Clinical Pharmacology & Therapeutics*, *6*, 279–291.

Feder, A., Parides, M. K., Murrough, J. W., Perez, A. M., Morgan, J. E., Saxena, S., . . . Charney, D. S. (2014). Efficacy of intravenous ketamine for treatment of chronic posttraumatic stress disorder: A randomized clinical trial. *JAMA Psychiatry*, *71*(6), 681–688.

Friedman, J. I., Soleimani, L., McGonigle, D. P., Egol, C., & Silverstein, J. H. (2014). Pharmacological treatments of non-substance-withdrawal delirium: A systematic review of prospective trials. *The American Journal of Psychiatry*, *171*(2), 151–159.

Gibbons, S. (2012). "Legal highs"—novel and emerging psychoactive drugs: A chemical overview for the toxicologist. *Clinical Toxicology (Philadelphia, PA)*, *50*(1), 15–24.

Green, S. M., Roback, M. G., Kennedy, R. M., & Krauss, B. (2011). Clinical practice guideline for emergency department ketamine dissociative sedation: 2011 update. *Annals of Emergency Medicine*, *57*(5), 449–461.

Hassan, Z., Bosch, O. G., Singh, D., Narayanan, S., Kasinather, B. V., Seifritz, E., . . . Müller, C. P. (2017). Novel psychoactive substances-recent progress on neuropharmacological mechanisms of action for selected drugs. *Frontiers in Psychiatry*, *8*, 152.

Honey, R. A., Honey, G. D., O'Loughlin, C., Sharar, S. R., Kumaran, D., Bullmore, E. T., . . . Fletcher, P. C. (2004). Acute ketamine administration alters the brain responses to executive demands in a verbal working memory task: An FMRI study. *Neuropsychopharmacology*, *29*(6), 1203–1214.

Honey, R. A., Turner, D. C., Honey, G. D., Sharar, S. R., Kumaran, D., Pomarol-Clotet, E., . . . Fletcher, P. C. (2003). Subdissociative dose ketamine produces a deficit in manipulation but not maintenance of the contents of working memory. *Neuropsychopharmacology*, *28*(11), 2037–2044.

Hopper, A. B., Vilke, G. M., Castillo, E. M., Campillo, A., Davie, T., & Wilson, M. P. (2015). Ketamine use for acute agitation in the emergency department. *The Journal of Emergency Medicine*, *48*(6), 712–719.

Jakobsen, C. J., Torp, P., Vester, A. E., Folkersen, L., Thougaard, A., & Sloth, E. (2010). Ketamine reduce left ventricular systolic and diastolic function in patients with ischaemic heart disease. *Acta Anaesthesiologica Scandinavica*, *54*(9), 1137–1144.

Kavalali, E. T., & Monteggia, L. M. (2012). Synaptic mechanisms underlying rapid antidepressant action of ketamine. *The American Journal of Psychiatry*, *169*(11), 1150–1156.

Lodge, D., & Mercier, M. S. (2015). Ketamine and phencyclidine: The good, the bad and the unexpected. *British Journal of Pharmacology*, *172*(17), 4254–4276.

Long, B. J., & Koyfman, A. (2018). Benign headache management in the emergency department. *The Journal of Emergency Medicine*, *54*(4), 458–468.

Maher, D. P., Chen, L., & Mao, J. (2017). Intravenous ketamine infusions for neuropathic pain management: A promising therapy in need of optimization. *Anesthesia & Analgesia*, *124*(2), 661–674.

Melamed, E., Oron, Y., Ben-Avraham, R., Blumenfeld, A., & Lin, G. (2007). The combative multitrauma patient: A protocol for prehospital management. *European Journal of Emergency Medicine*, *14*(5), 265–268.

Newcomer, J. W., Farber, N. B., & Olney, J. W. (2000). NMDA receptor function, memory, and brain aging. *Dialogues in Clinical Neuroscience*, *2*(3), 219–232.

Newport, D. J., Carpenter, L. L., McDonald, W. M., Potash, J. B., Tohen, M., & Nemeroff, C. B.; APA Council of Research Task Force on Novel Biomarkers and Treatments. (2015). Ketamine and other NMDA antagonists: Early clinical trials and possible mechanisms in depression. *The American Journal of Psychiatry*, *172*(10), 950–966.

Oovntan, S. A., & Gool, R. Y. (1970). Clinical trial of ketamine (CI-581): A preliminary report. *Canadian Journal of Anaesthesia*, *17*(4), 411–416.

Reinstatler, L., & Youssef, N. A. (2015). Ketamine as a potential treatment for suicidal ideation: A systematic review of the literature. *Drugs in R&D*, *15*(1), 37–43.

Riddell, J., Tran, A., Bengiamin, R., Hendey, G. W., & Armenian, P. (2017). Ketamine as a first-line treatment for severely agitated emergency department patients. *American Journal of Emergency Medicine*, *35*(7), 1000–1004.

Sin, B., Ternas, T., & Motov, S. M. (2015). The use of subdissociative-dose ketamine for acute pain in the emergency department. *Academic Emergency Medicine*, *22*(3), 251–257.

Singh, J. B., Fedgchin, M., Daly, E. J., De Boer, P., Cooper, K., Lim, P., . . . Van Nueten, L. (2016). A Double-blind, randomized, placebo-controlled, dose-frequency study of intravenous ketamine in patients with treatment-resistant depression. *The American Journal of Psychiatry*, *173*(8), 816–826.

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