Ketamine Use in Prehospital and Hospital Treatment of the Acute Trauma Patient: A Joint Position Statement [4/29/20]

ABSTRACT

The American College of Surgeons Committee on Trauma (ACS-COT), the American College of Emergency Physicians (ACEP), the National Association of State EMS Officials (NASEMSO), the National Association of EMS Physicians (NAEMSP) and the National Association of EMTs (NAEMT) have previously offered varied guidance on the use of ketamine in trauma patients. The following consensus statement represents the collective positions of the ACS-COT, ACEP, NASEMSO, NAEMSP and NAEMT. This updated uniform guidance is intended for use by emergency medical services (EMS) personnel, EMS medical directors, emergency physicians, trauma surgeons, nurses and pharmacists in their treatment of the trauma patient in both the prehospital and hospital setting.

INTRODUCTION

The American College of Surgeons Committee on Trauma (ACS-COT), the American College of Emergency Physicians (ACEP), the National Association of State EMS Officials (NASEMSO), the National Association of EMS Physicians (NAEMSP) and the National Association of EMTs (NAEMT) have previously offered independent and varied guidance on the use of ketamine in the trauma patient population. Ketamine is a non-competitive, N-methyl-D-aspartate receptor antagonist and potent dissociative agent with an evolving role in the management of both pediatric and adult trauma patients due to its sedative, anesthetic and analgesic properties. What follows is a consensus uniform guidance on the use of ketamine in the care of the trauma patient. It is intended for use by emergency medical services (EMS) personnel, EMS medical directors, emergency physicians, trauma surgeons, nurses and pharmacists in their treatment of the acute trauma patient both in and out of the hospital and within their respective domains. This document is not intended to be a comprehensive discussion of pain control options in the trauma patient. Instead, it combines the collective expertise of the author organizations with current published evidence to offer unified guidance on the role of ketamine in this patient population.

POINTS OF CONSENSUS

Indications

- 1. Analgesia
 - a. Ketamine is comparable to opioids and is less likely to decrease blood pressure or depress the respiratory system.
 - Ketamine is an appropriate analgesic for the trauma patient with moderate to severe pain in or at risk for developing hemorrhagic shock or respiratory distress.¹
 - c. Ketamine can potentiate the analgesic effect of opioids and may be given to trauma patients who are still in pain after receiving opioids or where re-dosing of opioids may be dangerous or harmful.

- d. Ketamine may be given to the trauma patient in whom opioids or other nonopioids are contraindicated.
- e. Ketamine is a reasonable option for the trauma patient taking buprenorphine/naloxone (Suboxone) for opioid use disorder.

2. Procedural Sedation

- a. Ketamine is preferable as a procedural sedation agent in patients with or at risk for hemorrhagic shock or respiratory distress or when procedures are expected to be brief in duration such as in the treatment of musculoskeletal injuries and burns.
- 3. Induction of Anesthesia/Rapid Sequence Intubation
 - a. The pharmacologic properties of ketamine make it excellent for use in hypotensive trauma patients for rapid sequence intubation (RSI) due to its hemodynamic, sedative and analgesic properties.
- 4. Acute Agitation/Excited delirium
 - a. Ketamine may be given to the trauma patient when acute control of agitation is required such as in patients with excited delirium or when rapid control is necessary to reduce the risk of injury to staff, bystanders or the patient themselves.

Contraindications

- 1. Use of ketamine in children less than 3 months of age is contraindicated as it has a higher incidence of airway complications and can lead to laryngospasm.
- 2. Ketamine should not be administered to patients with a known hypersensitivity reaction to the drug.
- 3. Ketamine is contraindicated in those in whom a significant elevation in blood pressure would constitute a serious hazard.²

Dosing

- 1. The dosing of ketamine in adults can be weight-based (based on ideal body weight) or non-weight-based. To better facilitate accuracy in children, ketamine dosing should always be weight or length based using a standardized measuring tape.
- 2. The sedative and analgesic effects of ketamine begin to wear off in 10-15 minutes.
- 3. There are no standard definitions for the dosing of ketamine. What follows are typical dosing guidelines based on review of the literature and expert opinion.
- 4. Analgesia dosing recommendations:
 - a. The terms low-dose, analgesic, pain control and sub-dissociative dose are frequently used interchangeably.
 - b. Intermittent dose:
 - i. 0.1-0.3 mg/kg (maximum 30mg) IV every 20 minutes prn for a maximum of 3 doses.
 - 1. This can be administered by slow IV push or as an IV piggyback over 10-15 minutes (associated with less feelings of unreality and sedation with no difference in analgesic efficacy).
 - ii. 0.5-1.0 mg/kg Intranasal (IN)

- c. Adult continuous infusion dose:
 - i. 0.1-0.4mg/kg/hour IV
- d. Adult non-weight based analgesic dosing:
 - i. 50mg IM, repeat every 30-60 minutes for pain control or until nystagmus develops indicating approach of the dissociative state.
 - ii. 20mg slow IV/IO push over 1 minute, repeat every 20 minutes for pain control or until nystagmus develops indicating approach of the dissociative state.
- 5. Procedural Sedation
 - a. 1mg/kg IV (maximum 100mg)
- 6. Induction of Anesthesia/RSI
 - a. 2mg/kg IV (maximum 200mg)
- 7. Acute Agitation/Excited delirium
 - a. 3-5 mg/kg IM
 - b. 1-2mg/kg IV
 - c. IV establishment in the acutely agitated patient or the patient with excited delirium is not recommended due to the elevated risk to the provider of occupational needle stick injury.
 - d. High-dose (5mg/kg) prehospital IM ketamine administration is associated with an increased intubation rate upon arrival to the hospital though the exact mechanism is difficult to elucidate.^{3,4} Providers administering high-dose ketamine should be prepared to secure the airway.
- 8. It is our opinion that doses between 0.5-0.9 mg/kg IV are not efficacious for sedation and can give patients a feeling of unreality that can lead to difficulties in patient management.

Safety

- Ketamine possesses profound analgesic properties while preserving cardiovascular stability, spontaneous respirations and protective airway reflexes and may be used as a safe and effective alternative or adjunct to opioids for pain control in the trauma patient.⁵
- 2. Due to its safety profile, administration of analgesic dose ketamine, should follow the same policies and procedures as other analgesic agents administered by nursing staff in the ED or other areas of the hospital.
- 3. It is our recommendation that ketamine use in the prehospital environment be approved by online or offline medical control prior to administration.
- 4. There is a lack of safety data to support recommendations regarding the use of ketamine in pregnancy and breast feeding.
- 5. Although previously discouraged, ketamine use can be considered in trauma patients with schizophrenia as there does not appear to be an associated increase in the incidence of psychosis.^{6,7}

Complications and Side Effects

- 1. Rapid IV injection can result in transient apnea. Ketamine should be administered slowly over 1 minute or greater unless being used in RSI where it is immediately followed by a neuromuscular blocking agent. Transient apnea following IM administration appears to be rare.²
- 2. Notable side effects include hypersalivation, laryngospasm, dysphoria, nausea, dizziness, nystagmus and emergence agitation. Most side-effects are transient and self-limited and do not require any intervention or rescue. If laryngospasm occurs, it can be managed with repositioning or jaw thrust and positive pressure ventilation. In rare instances, intubation may be necessary. End-tidal CO2 should be used if available to monitor for early signs of laryngospasm or hypoventilation.
- 3. Emergence reactions are felt to be rare. When they do occur, they can be safely managed with benzodiazepine administration. Pre-medicating with benzodiazepines is not recommended.

Ketamine and Head Injuries

- 1. Ketamine can safely be administered to the head-injured trauma patient as it has minimal effects on intracranial pressure (ICP) and has no adverse effect on cerebral perfusion pressure (CPP) or neurologic outcomes.^{8,9,10,11}
- 2. Though not contraindicated, ketamine induces a dissociative state which can make the neurologic monitoring of the head-injured patient difficult. Glasgow Coma Scale (GCS) should be documented prior to the administration of ketamine.

Ketamine and Eye Injuries

- 1. Ketamine-induced changes in intraocular pressure (IOP) are very slight and not clinically significant. The current Tactical Combat Casualty Care Guidelines do not preclude the use of ketamine in known or suspected open globe injuries. ¹⁴
- 2. Ketamine should not be used for procedural sedation to obtain an eye examination as one of the known side effects of ketamine is nystagmus.

Co-administration with other drugs

- When used in combination, ketamine potentiates the analgesic effects of opioids. The
 use of ketamine and opioids concomitantly allows for effective pain control with lower
 doses of opioids thus decreasing the likelihood of opioid-induced adverse effects on
 blood pressure or respirations.
- 2. Combining ketamine with opioids has been shown to block opioid-induced hyperalgesia and acute opioid tolerance.
- 3. When used in combination, ketamine potentiates the sedative effects of benzodiazepines. It is important to recognize the potential risks of respiratory decompensation when ketamine is used in combination with benzodiazepines. Extra caution should be exercised, airway monitoring should occur, and advanced airway management may be necessary.
- 4. Benzodiazepines should not be used prophylactically to prevent emergence reactions and should only be used to treat an emergence reaction if the patient is a danger to

themselves or staff. Suboptimal sedation requiring additional ketamine versus a true emergence reaction should be considered prior to benzodiazepine administration.

Considerations with non-prescribed drugs

- 1. Ketamine potentiates the sedative effects of alcohol and it is important to recognize the risks of respiratory decompensation when ketamine is administered to an acutely intoxicated patient. Advanced airway management may be necessary.³
- 2. Ketamine should be avoided if cocaine use is suspected as ketamine's sympathomimetic effects may potentiate the cardiovascular toxicity of cocaine.¹⁵

Geriatrics

 There is no good data regarding the use of ketamine in the elderly. Our consensus is to reduce the dose when using ketamine in the geriatric patient population since NMDA receptor binding is decreased with age.

Pediatrics

- 1. Ketamine is an alternative to opioids for sedation and analgesia-in the pediatric trauma patient over the age of 3 months.
- 2. Because of possible negative effects on the developing brain in infants who have received repeated or prolonged exposure to agents that block NMDA receptors, the use of ketamine in children less than 3 years of age should be weighed within the context of the benefits of procedures that require these agents.¹⁶
- 3. Prior to the administration of ketamine, it is first important to utilize adjunct measures for pain control such as immobilization of fractures or dislocations.
- 4. To better facilitate accuracy, ketamine administration in children should always be weight or length based using a standardized measurement tape.
- 5. Caution should be exercised when using ketamine in the prehospital setting in the head-injured child. Adverse effects of ketamine in the pediatric head injured trauma patient have not been reported in the literature, though evidence on this topic is limited.¹¹ Alternative medication and adjunct measures for pain control are well-established in this patient population.

CONCLUSION

This consensus document outlines the role of ketamine in the management of trauma patients in both the prehospital and hospital setting. Low-dose or sub-dissociative dose ketamine is a safe and effective analgesic that can be used for adult and pediatric trauma patients as an alternative to opioids, with opioids for synergistic effect, or for patients taking buprenorphine products with minimal effects on hemodynamic stability. Ketamine dissociative doses are safe and effective in adult and pediatric trauma patients and an excellent agent for induction of RSI, post-intubation sedation/analgesia and procedural sedation in the hypotensive trauma patient. Ketamine has a wide therapeutic window and thus can also be used for acute agitation and excited delirium. Ketamine analgesic dose policies and procedures should follow those of other analgesic agents administered by nursing staff in the emergency department. Ketamine use in the prehospital environment should be governed by local EMS policies and medical director

oversight. Further study on the use of ketamine in the adult and pediatric trauma patient population is warranted.

References:

- 1. Butler F, Kotwal R, Buckenmaier C, et al. *A triple-option analgesia plan for Tactical Combat Casualty Care: TCCC Guidelines Change 13-04.* J Spec Oper Med 2014; 14(1):13-25.
- 2. 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.
- 3. 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;33:76-9.
- 4. Hollis GJ, Keene TM, Ardlie RM, Caldicott DG, Stapleton SG. *Prehospital ketamine use by paramedics in the Australian Capital Territoy: A 12 month retrospective analysis.* Emergency Medicine Australasia. 2017;29:89-95.
- 5. Guldner G, Petinaux B, Clemens P, Foster S, Antoine S. *Ketamine for procedural sedation and analgesia by nonanesthesiologists in the field: a review for military health care providers.* J Mil Med 2006:171(6):484-90.
- 6. Lebin JA, Akhavan AR, Hippe DS, Gittinger MH, Pasic J, McCoy AM, Vrablik MC. *Psychiatric outcomes of patients with severe agitation following administration of prehospital ketamine*. Academic Emergency Medicine. 2019;26(8): 889-96.
- 7. Kudoh A, Katagai H, Takazawa T. *Anesthesia with ketamine, propofol, and fentanyl decreases the frequency of postoperative psychosis emergence and confusion in schizophrenic patients.*Journal of Clinical Anesthesia. 2002;14:107–110.
- 8. Albanese J, Arnaud S, Rey M, Thomachot, L, Alliez B, Martin C. *Ketamine decreases intracranial pressure and electroencephalographic activity in traumatic brain injury patients during Propofol sedation.* Anesthesiology. 1997;87(6):1328-1334.
- 9. Bowles ED, Gold ME. *Rethinking the paradigm: evaluation of ketamine as a neurosurgical anesthetic*. AANA J. 2013;81(1):18 and AANA J. 2012;80(6):445-452.
- 10. Zeiler FA, Teitelbaum J, West M, Gillman LM. *The ketamine effect on ICP in traumatic brain injury*. Neurocrit Care. 2014;21(1):163-173.
- 11. Hill GJ, April MD, Maddry JK, Schauer SG. *Prehospital ketamine administration to pediatric trauma patients with head injuries in combat theaters*. Am J Emerg Med. 2019 Aug;37(8):1455-1459.
- 12. Halstead SM, Deakyne SJ, Bajaj L, Enzenauer R, Rossevelt GE. *The effect of ketamine on intraocular pressure in pediatric patients during procedural sedation*. Academic Emergency Medicine. 2012;19(10): 1145-50.
- 13. Drayna PC, Estrada C, Wang W, Saville BR, Arnold DH. *Ketamine is not associated with clinically meaningful elevation of intraocular pressure*. Am J Emer Med. 2012;30(7):1215-18.
- 14. TCCC guidelines for Medical Personnel. J Special Operations Medicine 2017. Available at https://www.jsomonline.org/TCCC.html; accessed February 28, 2020.
- 15. Koehntop DE, Liao JC, Van Bergen FH. *Effects of pharmacologic alterations of adrenergic mechanisms by cocaine, tropolone, aminophylline, and ketamine on epinephrine-induced arrhythmias during halothane-nitrous oxide anesthesia*. Anesthesiology. 1977;46:83-93.

16. FDA Drug Safety Communication: FDA approves label changes for use of general anesthetic and sedation drugs in young children. Food and Drug Administration website. https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-fda-approves-label-changes-use-general-anesthetic-and-sedation-drugs. Accessed February 28, 2020.

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