

The Risks and Benefits of Prehospital Use of Ketamine

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Abstract

On August 24, 2019, Elijah McClain was unlawfully detained, and after two carotid holds by the police and a 500 mg injection of ketamine by Aurora Fire Rescue paramedics, he died in police custody. This literature review will discuss the benefits of prehospital use of ketamine, including short time to onset of effects and decreased risks of apnea and hypotension, as well as its risks, including hypersalivation, emergence reaction, laryngospasm, and high intubation rates.

Introduction: The Case of Elijah McClain

On February 22, 2021, almost 18 months after the death of Elijah McClain, an independent review panel commissioned by the Aurora City Council released their report on the incident and recommendations for the future. In their 157-page document, the commission detailed the death of McClain and concluded that police lacked the legal grounds to stop and forcefully detain him (Smith, 2021).

At 10:43 PM on August 24, 2019, Elijah McClain, who was walking back from a nearby convenience store to pick up iced tea, was stopped by the police due to a call of suspicious activity. Although the caller specifically stated that they had no suspicion that McClain was armed, the officers had their hands on the unarmed Black 23-year-old within 10 seconds of exiting their patrol car. With no attempt to deescalate, the officers performed 2 carotid holds, a method used to restrict blood flow to the brain so that

the subject temporarily loses consciousness. Mr. McClain was eventually rendered unconscious, and after one minute of not moving or making any sounds, EMS administered a 500 mg dose of ketamine to McClain. Based on his weight, the appropriate dose was 320 mg, but EMS overestimated McClain's weight by over 60 pounds and inappropriately rounded up to calculate the dose. Furthermore, EMS did not complete an initial assessment of McClain or a pre-sedation equipment check. At 11:01 PM, McClain was lifted onto a gurney. Cardiac monitors were not applied until after McClain was in the ambulance and already in cardiac arrest, 7 minutes after he received the ketamine. Although EMS was able to revive him, he was later declared brain dead. He was taken off life support less than a week later (Smith, 2021).

In response to public outcry, the city of Aurora has suspended the use of carotid holds and EMS use of ketamine. On the other

hand, the independent review panel stated that there was no “conclusive evidence that the ketamine administered to Mr. McClain was a direct cause of, or even contributed to, his death” or that accurate dosing would have changed the outcome (Smith, 2021). Furthermore, the autopsy report from the Adams County Coroner read:

“The manner of death may be accident if it was an idiosyncratic drug reaction. It may be natural if the decedent had an undiagnosed mental illness that led to Excited Delirium, if his intense physical exertion combined with a narrow coronary artery led to an arrhythmia, if he had an asthma attack, or if he aspirated vomit while restrained. It may be homicide if the actions of the officers led to his death (e.g. the carotid control held led to stimulation of the carotid sinus resulting in an arrhythmia). Based on my review of the EMS reports, hospital records, body-cam footage from the restraining officers, and the autopsy findings, I cannot determine which manner of death is most likely” (Broncucia-Jordan, 2019).

The Adams County coroner had actually met with Aurora police officers investigating McClain’s death before the autopsy report was released, and Aurora police investigators were even present during the autopsy, something that “should not happen,” according to state representative Leslie Herod (Sherry, 2021). Furthermore, an undetermined manner and cause of death is exceedingly rare in Colorado, with only 53 of 40,100 deaths having undetermined causes in 2019, according to the Colorado Department of Public Health and the Environment (Schmelzer, 2020).

Although ketamine may not have been the cause of Elijah McClain’s death according to the autopsy report or the independent review panel’s findings, it did play a role in the interaction between the police and Elijah McClain on the night of his death, and ketamine was a focal point of the reporting surrounding the incident. Furthermore, EMS use of ketamine is becoming more popular (Schmelzer, 2020). The Denver Post reports that 427 people were given ketamine for agitation from August 2017 to July 2018 by EMS statewide in Colorado, and twenty percent of those patients eventually had to be intubated at the hospital (Schmelzer, 2020). This literature review will summarize the use of out-of-hospital ketamine, as well as its risks and benefits.

The Use of Out-Of-Hospital Ketamine

Ketamine, which is classified as a dissociative agent, primarily acts as an antagonist on the NMDA receptors in the central nervous system. However, it also has activity at opioid sites and other neurotransmitter pathways. The FDA has currently approved ketamine for two indications: procedural sedation, like intubations, and general anesthesia in the operating room. However, ketamine is widely used off-label to rapidly sedate agitated patients and at lower doses for migraines, chronic pain, and even major depression (Kitch, 2020).

In a cross-sectional survey of paramedics in the US in 2017, 53% of the 10,737 surveyed paramedics reported

learning about ketamine during their training and 33% were authorized by protocol to use ketamine. One-third of the authorized providers had never used ketamine, but of the paramedics that had given the drug, 94% felt comfortable with its use and 95% would use it again in a similar situation. 72% of the authorized uses were for chemical restraint and sedation (Buckland, 2017).

The Benefits of Ketamine

First-line agents for acute agitation in adult patients include antipsychotics, benzodiazepines, opioids, or diphenhydramine. Most medications that can be used for sedation induce apnea and loss of airway reflexes, but because ketamine works through inducing dissociation from reality rather than unconsciousness, the patient can protect their airway and breathe on their own. Similarly, many sedating medications can cause cardiovascular side effects. Opioids, like fentanyl, cause hypotension, especially in unstable patients, and antipsychotics have the potential to induce arrhythmias in patients with QTc prolongation. On the contrary, ketamine has sympathomimetic properties, often increasing blood pressure and cardiac index. Furthermore, most sedating medications, such as antipsychotic drugs, benzodiazepines, and diphenhydramine, are on the Beers list, a frequently cited resource of medications that should be used with caution in the geriatric population. Ketamine is not on that list (Kitch, 2020).

Finally, the time to onset of effects is much shorter for ketamine (3-4 minutes IM)

compared to fentanyl/midazolam (10-15 minutes IM) or haloperidol (15-30 minutes IM). One prospective study assessed ketamine and haloperidol administration by paramedics as first-line therapy for severe agitation during two consecutive 6-month periods. 64 patients received ketamine, while 82 were given haloperidol. The median time to adequate sedation for patients given ketamine was 5 minutes, while the median time to sedation in the haloperidol group was 17 minutes (Cole, 2016).

The Risks of Ketamine

In the same study outlined above, complications occurred in 49% of patients who received ketamine, while only 5% of patients in the haloperidol group had any documented complications. Within the group of patients who received ketamine and had complications, 38% had hypersalivation, 10% had emergence reaction, or agitation and confusion upon waking up, 9% vomited, and 5% had laryngospasm. Furthermore, when the patients arrived at the hospital, 39% of the patients treated with ketamine were intubated, compared to 4% of patients who received haloperidol (Cole, 2016). Although the indication for intubation is often subjective and based off a low Glasgow Coma Score, even though a patient sedated with ketamine may be breathing normally, this does not account for the large discrepancy in intubation rates between the ketamine and haloperidol groups.

Another prospective observational study of ketamine use by EMS for patients with acute behavioral disturbance found that

40 of 105 patients had adverse events. Fifteen were over-sedated, four vomited, four had hypoxia, three had bradypnea, and two had emergence reactions. Sixteen patients were intubated (Isoardi, 2020).

A retrospective cohort study of all patients who received prehospital ketamine for profound agitation and who were transported to an urban Level 1 trauma center from May 2010 to August 2013 documented the indications for intubation. Throughout the study period, ketamine was administered to 227 patients, 63% of whom were intubated. Almost all intubations occurred in the hospital, although prehospital intubation was attempted in four cases. The primary indications for intubation included an unprotected airway (36%), hypersalivation (18%), respiratory failure (14%), hemodynamic instability (11%), hypoxia (4%), and status epilepticus (4%) (Olives, 2016).

Another retrospective, multi-site study analyzed whether higher doses of ketamine were associated with higher incidences of adverse events. Although this study only included adult subjects receiving ketamine for rapid sequence intubation, the fifty subjects who received high-dose ketamine (>2 mg/kg IV) were found to have greater odds of adverse events in comparison to the eighty subjects who received standard-dose ketamine (<2 mg/kg IV). This included hypotension (OR = 7.0; 95% CI, 3.0-16.6), laryngospasm (OR = 10.8; 95% CI, 1.3-93.4), bradycardia (OR = 7.5; 95% CI, 1.5-36.6), and oxygen desaturation (OR = 6.0; 95% CI, 1.8-19.9) (Krebs, 2021).

Excited Delirium

The indication that Aurora EMS gave for administering ketamine to Elijah McClain was “excited delirium,” and that same term came up in Mr. McClain’s autopsy report. Because the management of excited delirium is rapid chemical sedation, most often ketamine, this review will discuss the implications of this diagnosis.

Although the term “excited delirium” was first used in 1985, similar terms like “Bell’s mania” have been used since the mid-1800s. The diagnosis often describes patients with delirium and agitation, including shouting, violence, and hyperactivity, often followed with a sudden cessation of struggle, respiratory arrest, and death (Gonin, 2017). Because there are no autopsy findings that indicate excited delirium, and because intoxicant levels are typically far below overdose levels, the diagnosis is one of exclusion and is often controversial, especially when restraint is used at the time of death. This is especially true as positional or compressive asphyxia from restraint also has no specific findings at autopsy. Furthermore, excited delirium is not currently recognized as a diagnosis by the American Psychiatric Association, the American Medical Association, or the World Health Organization and is not listed in the DSM-V or the International Classification of Diseases (ICD-9) (Stommer, 2020).

A meta-analysis was done that narrowed down 61 studies according to their criteria, which provided detailed information about 168 total cases of excited delirium.

95.8% of cases involved men, 25% involved a person with at least one mental health diagnosis, 87% involved some drug intoxication, and 82% involved use of police force. Interestingly, 90% of cases that resulted in death involved some form of restraint. In contrast, only 67% of cases where the person survived involved restraint (Strommer, 2020).

On the other hand, another review of reported case series attempted to draw conclusions about the pathophysiology of excited delirium. Although the majority of cases of excited delirium involved use of stimulants, most often cocaine, the blood levels of cocaine in excited delirium cases are similar to recreational cocaine users and much lower than levels of cocaine overdose deaths (Takeuchi, 2011). Furthermore, a large case series from 2006 noted that the majority of fatal cases of excited delirium had some degree of cardiovascular disease, such as hypertrophy, microangiopathy, and myocardial fibrosis, possibly due to long-term cocaine use and catecholamine stress on the heart. During times of increased stress, such as force by the police, the myocardium may be more susceptible to ischemia (Takeuchi, 2011). Of note, Elijah McClain had no evidence of cocaine or any other stimulant drug in his blood.

Conclusion

Ketamine may serve a purpose in ensuring the safety of both paramedics and agitated patients, but the risk of adverse events is high and should be taken seriously. The FDA plans to issue guidance on pre-hospital ketamine use by the end of 2021,

which may impact the policies of EMS systems nationwide (Smith, 2021).

As calls for defunding the police and instead investing in community programs, including mental health systems, continue to echo, the healthcare community must look within to assess our own implicit biases and frameworks of institutional racism. Although we do not know if ketamine was what killed Elijah McClain, implicit bias from the healthcare system was prevalent throughout that interaction on August 24, 2019, from overestimating McClain's weight by over 60 pounds to diagnosing him with excited delirium without a proper evaluation. To emphasize the true tragedy of Elijah McClain's death, this paper will conclude with his last words (Smith, 2021).

"I can't breathe. I have my ID right here. My name is Elijah McClain. That's my house. I was just going home. I'm an introvert. I'm just different. That's all. I'm so sorry. I have no gun. I don't do that stuff. I don't do any fighting. Why are you attacking me? I don't even kill flies! I don't eat meat! But I don't judge people, I don't judge people who do eat meat. Forgive me. All I was trying to do was become better. I will do it. I will do anything. Sacrifice my identity, I'll do it. You all are phenomenal. You are beautiful and I love you. Try to forgive me. I'm a mood Gemini. I'm sorry. I'm so sorry. Ow, that really hurt! You are all very strong. Teamwork makes the dream work. Oh, I'm sorry, I wasn't trying to do that. I just can't breathe correctly."

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