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WHITE PAPER

Ketamine for the Patient with Excited Delirium

BACKGROUND

Excited delirium, a condition with high risk of morbidity and mortality, also presents a practical and logistic dilemma for first responders and healthcare providers, as these patients are irrational and often combative. This not only increases morbidity and mortality for the patient, but also places healthcare providers at risk of injury as well. It is important to have the proper tools to manage these patients in order to protect law enforcement, EMS providers, bystanders, emergency department personnel and the patients themselves

DEFINITION and CHARACTERISTICS

Excited delirium is a syndrome of metabolic, neurologic and behavioral changes characterized by tachypnea, high pain tolerance, "bizarre and aggressive behavior, shouting, paranoia, panic, violence toward others, unexpected physical strength, and hyperthermia"[1], followed by sudden cessation of struggle, respiratory arrest and death[2,3]. This condition is most often associated with methamphetamine, cocaine or other substance abuse, particularly "bath salts", or synthetic cathinones (khat). However, it has also been reported in cases of extreme psychiatric illness, such as schizophrenia or bipolar illness, in the absence of substance abuse[4].

It is thought that excited delirium results from a dysregulation of neurotransmitters, particularly dopamine, and that patients with excited delirium have underlying neurotransmitter vulnerabilities that may predispose them to developing this condition [1,2]. Some of these underlying vulnerabilities may preexist the substance abuse, and some of the them may be as a result of remodeling in the brain over the course of chronic substance abuse.

In 1995, Stratton et al reported that 2/3 of excited delirium patients die at the scene or during transport by paramedics or police [5]. Those who survive to the hospital often develop disseminated intravascular coagulation, rhabdomyolysis and renal failure [6]. In particular, the use of the "hog tie" form of restraint, in which the patient's hands and feet are bound together behind the back, increases the risk of cardiovascular collapse. Some have proposed that the mechanism for the cardiovascular collapse is anoxic brain death from positional asphyxia [4, 7]. However, this theory has been refuted. Many authors have argued that the mechanisms for cardiovascular collapse are likely quite complex[8], and extensive discussion of these mechanisms is outside the scope of this white paper.

TREATMENT

No matter the exact mechanism, rapid sedation and transport are essential to good outcomes. Some typical sedating agents that have been used are haloperidol, lorazepam, midazolam and other benzodiazepines and/ or neuroleptics. While these medications have had some success in moderating the behavior of patients with excited delirium, they are not without potential negative side effects, such as respiratory depression and prolonged time to onset. Prolonged time to onset of action is particularly troublesome in these patients because the longer the patient struggles against physical restraints, the higher the risk of cardiovascular collapse.

Ketamine, which has a long track record in the operating room and the emergency department, has been suggested as a reasonable choice for use in the field for management of these patients, when given in dissociative doses [2]. It offers the benefit of rapid onset within three to four minutes when given intramuscularly (IM), and about thirty seconds when given intravenously (IV). Ketamine has predictable and reliable dissociative and sedating effects, as well as minimal negative effect on respiratory drive, heart rate and blood pressure.

Many authors have reported their experience using ketamine in the prehospital setting, achieving excellent rates of adequate sedation [11-14]. Ketamine offers a level of sedation at least as good as or better than other agents currently used, such as haloperidol. However, some authors have reported levels of intubation that are higher than reported rates when ketamine is used in the emergency department for procedural sedation [11-14]. The reason for this is unclear, and research is ongoing. One possibility is that the receiving facility was unfamiliar with the presentation of a patient sedated with ketamine. Another possibility is that the typical patient with excited delirium has multiple abuse substances on board, and that the combination of ketamine with these other substances increases the need for respiratory support. In any case, ketamine remains a reasonable choice despite the reported levels of intubation, given the very high-risk nature of excited delirium, the pressing need for sedation in a timely manner, and the risks and side effects of the other restraint and sedation options [3,10].

In 2015 the American College of Emergency Physicians Board of Directors approved ketamine for use in excited delirium

> "Ketamine, given in dissociative doses, can provide rapid onset of chemical sedation in extremely violent patients, particularly those with excited delirium, minimizing the risk of further harm to the patient or rescuers. It provides a rapid and effective hemodynamically stable sedation while leaving airway reflexes intact. It has been reported to cause laryngospasm in rare cases. EMS personnel should be adequately prepared to recognize and manage this condition" [10]

Ketamine can be administered IM (4 mg/kg/dose) with onset of action of three to four minutes, or IV (1-2 mg/kg/dose) with onset of action of 30 seconds. It does not typically require endotracheal intubation, though providers should be prepared to manage the airway if needed.

The use ketamine in agitated patients should be limited to those with excited delirium. The "Altered Mental Status Scale" (AMSS) has been developed to assist in the identification of patients with excited delirium. This scale is intended to identify patients with agitated delirium as well as severe depressions in mental status and progresses from -4 (non-responsive, speaking few recognizable words, glazed eyes with ptosis) to + 4 in which the patient is combative, violent, loud agitated with no ptosis. The MDPB suggests use of this scale to assist in proper patient selection. The scale is included below for reference and will be included in the 2017 "Agitation/Excited Delirium" protocol in the Yellow Section. Patients who score a +1, +2, or +3 may be treated as in prior protocols and receive midazolam, without the need to contact OLMC. Patients scoring a +4 may receive midazolam without contacting OLMC or may receive ketamine 4 mg/kg IM after contacting OLMC. As mentioned above, patients suffering alcohol or sedative intoxication may have additive respiratory depression. Consider using a half dose of ketamine in these settings to minimize respiratory depression. Additionally, many sources document additive respiratory depression when benzodiazepines and ketamine are used together at the doses mentioned in the Agitation/Excited Delirium protocol. Once a therapeutic pathway in initiated, therapy should continue with increased doses of the first medication chosen rather than adding an alternate medication. Please refer to OLMC for dosing questions or if the patient requires additional doses of medication.

Score	Responsiveness	Speech	Facial Expression	Eyes
+4	Combative, very violent, out of control	Loud Outbursts	Agitated	Normal
+3	Very anxious, agitated, mild physical element of violence	Loud Outbursts	Agitated	Normal
+2	Anxious, agitated	Loud Outbursts	Normal	Normal
+1	Anxious, restless	Normal	Normal	Normal
0	Responds readily to name in normal tone	Normal	Normal	Clear, no ptosis
-1	Lethargic response to name	Mild slowing or thickening	Mild relaxation	Glazed or mild ptosis (< Half eye)
-2	Responds only if name is called looudly	Slurring or prominent slowing	Mild relaxation (slacked jaw)	Glazed and marked ptosis (> half eye)
-3	Responds only after mild prodding	Few recognizable words	Mild relaxation (slacked jaw)	Glazed and marked ptosis (> half eye)
-4	Does not respond to mild prodding or shaking	Few recognizable words	Mild relaxation (slacked jaw)	Glazed and marked ptosis (> half eye)

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