Rescue Intubation in the Emergency Department After Prehospital Ketamine Administration for Agitation

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Conflicts of interest: The authors report no conflict of interest.

Keywords: airway management; delirium; intubation; ketamine; psychomotor agitation

Abbreviations:
ED: emergency department
EMR: electronic medical record
EMS: Emergency Medical Services
GCS: Glasgow Coma Score
IM: intramuscular
IO: intraosseous
IV: intravenous
NC: nasal cannula
REDCap: Research Electronic Data Capture

Received: May 14, 2020
Revised: June 21, 2020
Accepted: June 25, 2020

doi:10.1017/S1049023X20001168

Abstract

Objective: Prehospital intramuscular (IM) ketamine is increasingly used for chemical restraint of agitated patients. However, few studies have assessed emergency department (ED) follow-up of patients receiving prehospital ketamine for this indication, with previous reports suggesting a high rate of post-administration intubation. This study examines the rate of and reasons for intubation and other airway interventions in agitated patients who received ketamine by Emergency Medical Services (EMS).

Methods: This retrospective cohort study included patients who received prehospital ketamine for agitation and were transported to two community hospital EDs. Charts were reviewed for demographics, ketamine dose, and airway intervention by EMS or in the ED. Characteristics of patients who were intubated versus those who did not receive airway intervention were analyzed.

Results: Over 28 months, 86 patients received ketamine for agitation. Fourteen (16.3%) underwent endotracheal intubation. Patients with a higher temperature and a lower Glasgow Coma Score (GCS) were more likely to require intubation. There was no age or dose-dependent association on intubation rate. Intubated patients averaged 39 years old versus 44 for patients not intubated (negative five-year difference; 95% CI, -16 to 6). The mean ketamine dose was 339.3mg in patients intubated versus 350.7mg in patients not (-11.4mg difference; 95% CI, -72.4 to 49.6). The mean weight-based ketamine dose was 4.44mg/kg in patients intubated versus 4.96mg/kg in patients not (-0.53mg/kg difference; 95% CI, -1.49 to 0.43).

Conclusions: The observed rate of intubation in patients receiving prehospital ketamine for agitation was 16.3%. Study data did not reveal an age or dose-dependent rate of intubation. Further research should be conducted to compare the airway intervention rate of agitated patients receiving ketamine versus other sedatives in a controlled fashion.

Parks DJ, Alter SM, Shih RD, Solano JJ, Hughes PG, Clayton LM. Rescue intubation in the emergency department after prehospital ketamine administration for agitation. *Prehosp Disaster Med.* 2020;35(6):651–655.

Introduction

Both prehospital and emergency department (ED) health care providers encounter violent, combative, and agitated patients on a regular basis.[1] This can pose safety risks to both the patient and the provider. To deter such risks, certain chemical restraints have been used in the past such as benzodiazepines, anticholinergics, and antipsychotics.[2] Ketamine is a N-methyl-D-aspartate (NMDA) receptor blocker that produces a dissociative state without respiratory depression at higher doses, which can be administered via intramuscular (IM), intranasal (IN), intraosseous (IO), or intravenous (IV) routes.[3]

Recently, Emergency Medical Services (EMS) providers have been increasingly using ketamine as a chemical restraint due to its rapid onset of action, safety profile, and the ability for the patient to maintain respiratory drive.[4] Within the study's geographic area, ketamine has become the most frequently used sedative agent. Local EMS protocols allow for ketamine administration in violent/combative patients and suspected excited delirium. Under standing orders, paramedics commonly administer ketamine at a standardized dose of 400mg IM or 200mg IV/IO, with the ability to repeat the dose once as needed.

However, few studies have examined the use of ketamine for agitation, including dose-dependent outcomes, and results have varied regarding rate of intubation and other adverse

outcomes.[4-10] The goal of this study was to evaluate the safety of prehospital ketamine administration, as determined by the rate of airway intervention after ketamine administration, including the need for intubation.

Methods

Study Design and Setting

This is a retrospective cohort study of patients transported by EMS to the EDs of two community hospitals. The combined annual volume of both EDs is over 81,000 visits per year. Multiple fire-based EMS agencies, operating under the same standing orders, transport patients to the two hospitals. The study was approved by the institutional review boards of Florida Atlantic University (Boca Raton, Florida USA; study #1100947) and Baptist Health South Florida (Miami, Florida USA; study #1308933).

Selection of Participants

Patients receiving ketamine by EMS and transported to one of the study hospitals from January 1, 2017 through April 30, 2019 were identified. Inclusion criteria were age 18 or greater and ketamine administration by EMS for agitation. Patients were excluded if they solely received ketamine as an induction agent for intubation, as post-intubation sedation, or for pain control.

Measurements

The hospitals' health information management department ran a query that retrieved patients 18 years and older who had the keyword "ketamine" mentioned in either the ED physician or nursing documentation from January 1, 2017 through April 30, 2019. Chart review of the patients' hospital electronic medical record (EMR) and prehospital EMS report was conducted by one of the physician study investigators, who was aware of the research question. Charts were first screened for ketamine administration reason prior to full-chart review. Only patients who were treated with ketamine for agitation were included. Any unclear reason for ketamine administration was adjudicated by a second study investigator.

Variables extracted from the charts included demographic data such as age and gender, as well as height and weight from the ED triage note. First documented EMS vital signs and first documented ED vital signs were recorded, as well as dose, route, and indication for ketamine administration. If the EMS report was not available, ketamine administration information was obtained from nurse and physician documentation of prehospital treatment. Patient history, including medical history and social history, were also recorded. Airway interventions (intubation, supraglottic airway placement, supplemental oxygen administration, oral/nasal airway placement, and airway suctioning) were noted if performed by either EMS or ED personnel, as well as indication(s) for performance of each intervention as documented in the narrative reports. Finally, any concomitant use of additional sedatives besides ketamine was identified if administered by EMS or in the ED.

Study data were systematically collected using the Research Electronic Data Capture (REDCap; Vanderbilt University; Nashville, Tennessee USA) data management system.[11] Variables were abstracted directly from the EMR to the web-based data collection instrument, which used real-time validation to ensure accuracy of data entry.

Outcomes

The primary outcome measure was need for airway intervention, with intubation being the main focus. Additional airway interventions included supplemental oxygen administration, need for airway suctioning, placement of an oral/nasal airway, and placement of a supraglottic airway. Secondary outcomes included patient disposition from the ED (admit, discharge, or transfer).

Analysis

Patients were stratified into two groups based on if they necessitated intubation after ketamine administration. Mean ketamine doses were compared between the groups by independent samples T-tests. Proportions of patients intubated by reasons for agitation, comorbidities, and exam findings were compared using chi-squared tests. Using data directly exported from REDCap, statistical analyses were conducted using SPSS (IBM Corporation; Armonk, New York USA).

Results

Characteristics of Study Subjects

During the 28 months of data review, 254 patients were identified with "ketamine" mentioned in their ED charts. One hundred sixty-eight had ketamine mentioned for reasons other than for administration by EMS for agitation. Of these, 53 received ketamine by EMS for other indications (47 for pain management, five for intubation induction, and one for post-intubation sedation); 74 received ketamine in the ED; and 41 had ketamine mentioned on their chart but not administered (23 allergy, nine home medication, five abuse history, and four other). The remaining 86 patients were enrolled in the study. Forty-seven (54.7%) were female and the average age was 42.9 years (SD = 18.9; range 18 to 98). Ketamine was administered primarily via IM (97.6%). Doses of ketamine ranged from 50mg to 600mg (mean 349; SD = 104). Weight-based doses of ketamine ranged from 0.74mg/kg to 8.80mg/kg (mean 4.88; SD = 1.65). Two patients were missing route of administration and one was missing the dose administered. These patients were only excluded from dosing analyses.

Main Results

Fourteen of 86 patients (16.3%) underwent endotracheal intubation while in the ED. One of these patients underwent bag-valve-mask ventilation and unsuccessful intubation attempt by EMS after ketamine administration. No other patients had invasive airway management by EMS after ketamine administration. Patients undergoing intubation had a variety of indications for this procedure, including decreased Glasgow Coma Scale (GCS; 43.0%), respiratory failure (43.0%), hypoxia (36.0%), hypercarbia (13.9%), vomiting (6.9%), airway protection (63.9%), hypersalivation (6.9%), and need for paralysis (13.9%).

The mean ketamine dose of the intubation group was 339.3mg (95% CI, 293.7 to 384.8) and mean dose of the group that was not intubated was 350.7mg (95% CI, 324.9 to 376.5), which was not significantly different (-11.4mg difference; 95% CI, -72.4 to 49.6; P = .711). There was no significant difference in the weight-based dosing between groups, which was 4.44mg/kg (95% CI, 3.73 to 5.15) in the intubation group and 4.96mg/kg (95% CI, 4.56 to 5.37) in the non-intubated group (-0.53mg/kg difference; 95% CI, -1.49 to 0.43; P = .278).

The EMS temperature, ED temperature, and ED GCS were all significantly different between the group that was intubated and the group that was not: EMS temperature = 38.6°C versus 37.0°C (1.6°C difference; 95% CI, 0.6 to 2.6; P = .003); ED temperature = 38.0°C versus 37.1°C (0.8°C difference; 95% CI, 0.3 to 1.4; P = .005); and ED GCS = 5.6 versus 10.4 (-4.7 difference; 95% CI, -6.9 to -2.6; P <.001). No other vital signs from EMS or the ED

https://doi.org/10.1017/S1049023X20001168 Published online by Cambridge University Press

	Intubated				
	Yes	No	Difference	(95% CI)	P Value
	N = 14	N = 72			
Ketamine Dose (mg)	339	351	−11	(−72 to 50)	.711
Ketamine Weight-Based Dose (mg/kg)	4.4	5.0	−0.5	(−1.5 to 0.4)	.278
Age (years)	39	44	−5	(−16 to 6)	.352
EMS Heart Rate (/min)	114	104	11	(−8 to 29)	.252
EMS Respiratory Rate (/min)	17	19	−2	(−7 to 2)	.332
EMS Pulse Ox (%)	97	96	0.5	(−3 to 4)	.803
EMS Systolic Blood Pressure (mmHg)	141	150	−9	(−33 to 14)	.426
EMS Diastolic Blood Pressure (mmHg)	89	92	−3	(−18 to 13)	.743
EMS Temperature (C)	38.6	37.0	1.6	(0.6 to 2.6)	.003
EMS EtCO2 (mmHg)	54	35	19	(−3 to 41)	.092
ED Temperature (C)	38.0	37.1	0.8	(0.3 to 1.4)	.005
ED Systolic Blood Pressure (mmHg)	140	145	−6	(−25 to 13)	.556
ED Diastolic Blood Pressure (mmHg)	79	84	−5	(−17 to 8)	.453
ED Heart Rate (/min)	115	108	6	(−8 to 20)	.377
ED Respiratory Rate (/min)	21	19	2	(−1 to 6)	.184
ED Pulse Ox (%)	97	96	0.2	(−4 to 5)	.944
ED GCS Total	5.6	10.4	−4.7	(−6.9 to -2.6)	<.001

Table 1. Characteristics by Intubation
Abbreviations: ED, emergency department; EMS, Emergency Medical Services; EtCO2, end-tidal CO2; GCS, Glasgow Coma Score.

	Intubated				
Agitation Reason	Yes	No	Difference	(95% CI)	P Value
	N = 14	N = 72			
Acute Psychosis	0 (0%)	9 (13%)	-13%	(-22 to 10)	.344
Alcohol Intoxication	1 (7%)	15 (21%)	-14%	(-26 to 12)	.452
Drug Intoxication	7 (50%)	28 (39%)	11%	(-15 to 37)	.555
Excited Delirium	7 (50%)	28 (39%)	11%	(-15 to 37)	.555
Postictal Confusion	2 (14%)	5 (7%)	7%	(-6 to 33)	.319
Violent/Combative	7 (50%)	53 (74%)	-24%	(-48 to 2)	.111

Table 2. Reason for Agitation by Intubation, n (%)

	Intubated				
Comorbidity	Yes	No	Difference	(95% CI)	P Value
	N = 14	N = 72			
Other Sedative Administered	6 (43%)	29 (40%)	3%	(−22 to 29)	1.000
Cardiovascular Disease[a]	4 (29%)	21 (29%)	−0.6%	(−21 to 27)	1.000
Pulmonary Disease[b]	1 (7%)	5 (7%)	0.2%	(−10 to 25)	1.000

Table 3. Risk Factors by Intubation, n (%)
[a] Atrial fibrillation, congestive heart failure, coronary artery disease, hypertension, and valvular disease.
[b] Asthma, chronic obstructive pulmonary disease, and pulmonary hypertension.

demonstrated statistically significant differences between the two groups (Table 1).

There was no difference between the group that was intubated versus the group that was not in regard to age, cause of agitation (acute psychosis, alcohol intoxication, drug intoxication, excited delirium, postictal confusion, or violence/combativeness), patient's comorbidities (cardiovascular disease or pulmonary disease), or being treated with additional sedation in addition to ketamine (Table 2 and Table 3).

Certain clinical exam findings by the ED physician had significantly increased rate of intubation including abnormal lung sounds (29% versus 3%, 26% difference; 95% CI, 8 to 52; P = .006),

https://doi.org/10.1017/S1049023X20001168 Published online by Cambridge University Press

Exam Finding	Intubated		Difference	(95% CI)	P Value
	Yes	No			
	N = 14	N = 71[a]			
Abnormal Lung Sounds	4 (29%)	2 (3%)	26%	(8 to 52)	.006
Respiratory Distress	8 (57%)	0 (0%)	57%	(32 to 79)	<.001
Apnea	3 (21%)	1 (1%)	20%	(5 to 46)	.013
Agitation	4 (29%)	20 (28%)	0.4%	(-20 to 28)	1.000
Vomiting	1 (7%)	0 (0%)	7%	(-0.7 to 31)	.165
Hypersalivation	1 (7%)	1 (1%)	6%	(-3 to 30)	.304
Protecting Airway	6 (43%)	70 (99%)	-56%	(-77 to -30)	<.001

Table 4. Emergency Department Physical Exam Findings by Intubation, n (%)
[a] One patient had physical exam missing from emergency department physician note.

respiratory distress (57% versus 0%, 57% difference; 95% CI, 32 to 79; P = <.001), apnea (21% versus 1%, 20% difference; 95% CI, 4 to 46; P = .013), and if the patient was protecting their airway (43% versus 99%, -56% difference; 95% CI, -77 to -30; P = <.001). Findings of agitation, vomiting, and hypersalivation while the patients were in the ED were not associated with an increase in intubation (Table 4).

In addition to the 14 patients intubated, one patient had a nasopharyngeal airway placed and required oral suction. Another had an oropharyngeal airway placed that was removed shortly after naloxone was administered. Twenty-one of the patients that did not get intubated received supplemental oxygen in the ED (16.3% nasal cannula [NC], 8.1% nonrebreather [as well as NC], and 1.2% venti mask). Only six of these patients had one or more documented reasons for supplemental oxygen (three for decreased GCS, two for respiratory distress/failure, four for hypoxia, one for hypercapnia, and one for hypersalivation).

Of the 86 patients, 66 (76.7%) were medically admitted to the hospital, 16 (18.6%) were discharged, and four (4.7%) were transferred to a psychiatric facility.

Discussion

This study's rate of intubation of 16% is considerably lower than most previous studies.[5-7] There is a wide range of intubation rate associated with prehospital ketamine for agitation. A retrospective study of 135 patients demonstrated an intubation rate of 63%, concluding that this high rate may be associated with provider variability in comfort level with post-ketamine patients.[6] A retrospective Australian study found that of 38 patients who received prehospital ketamine for agitation, 26% required intubation.[10] In a prospective study of 146 patients (64 of which received ketamine), 39% of the ketamine group received intubation.[5] The authors also felt that there was significant variation in provider comfort with post-ketamine patients and they suggested that patients receiving ketamine should be scored in a different manner regarding GCS evaluation. Patients who are dissociated with ketamine often have a GCS of three due to the effects of the medication. However, unlike most other unresponsive patients who typically require intubation, patients who receive ketamine often have maintained airway reflexes, respiratory drive, and cardiovascular stability.

Contrary to the studies mentioned above, others have reported a much lower rate of intubation following ketamine administration. The lowest published rate of prehospital intubation was four percent in a retrospective review of 52 patients receiving ketamine for agitated delirium by EMS, but the study did not evaluate subsequent care in the ED, where most of the patients requiring intubation in this study was performed.[12] A prospective study of 49 patients who received rescue ketamine after failing droperidol for agitated delirium demonstrated no cases of intubation, with a 300mg median dose of ketamine and 50mg to 500mg range.[13]

Some studies have shown an association between higher doses of ketamine and intubation.[4] However, other studies fail to demonstrate such an association.[5,6] This study's data fail to demonstrate association of dose, route, age, any vital signs (other than temperature), intoxication, comorbidities, or additional sedatives with risk of intubation. There was a significant difference in patients with a higher temperature and a lower GCS in the group that were intubated, perhaps representing a sicker cohort of patients.

Twenty-one patients that did not get intubated did receive supplemental oxygen in some form; however, at the study institution, it is common practice for nurses to place sedated patients on oxygen even in the absence of clinical necessity. Reason for oxygen administration was not consistently documented, and it is uncertain what percentage of these patients truly needed it.

Limitations

There were several limitations to this study. The retrospective nature of this study is prone to selection bias. Some charts were lacking EMS documentation. In these cases, the physician and nursing documentation were used to determine indication, dose, route, and circumstances of ketamine administration. This may have led to inaccuracies, insufficient data, or failure to identify patients who received this intervention. In addition, where GCS was not reported, this was estimated based on available documentation in the chart. There were multiple instances where supplemental oxygen was administered without a documented indication or a clear reason from chart review by both EMS and in the ED. It is unclear whether these patients required oxygen, or if it was simply administered as prophylaxis in a patient who had received sedation. In addition, neither hospital in the study has a psychiatric facility and thus EMS may have preferentially transported patients with acute psychosis/agitated delirium to a more distant hospital equipped with psychiatric services.

Conclusions

The observed rate of intubation in patients receiving prehospital ketamine for agitation was 16.3%. Patients with a higher temperature

https://doi.org/10.1017/S1049023X20001168 Published online by Cambridge University Press

and a lower GCS were more likely to require intubation. Study data did not reveal an age or dose-dependent rate of intubation. Further research should be conducted to compare the airway intervention rate of agitated patients receiving ketamine versus other sedatives in a controlled fashion and other less-objective factors such as clinician experience and comfort.

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