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Original Contribution

Ketamine as a first-line treatment for severely agitated emergency department patients☆

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ABSTRACT

Objective: Emergency physicians often need to control agitated patients who present a danger to themselves and hospital personnel. Commonly used medications have limitations. Our primary objective was to compare the time to a defined reduction in agitation scores for ketamine versus benzodiazepines and haloperidol, alone or in combination. Our secondary objectives were to compare rates of medication redosing, vital sign changes, and adverse events in the different treatment groups.
Methods: We conducted a single-center, prospective, observational study examining agitation levels in acutely agitated emergency department patients between the ages of 18 and 65 who required sedation medication for acute agitation. Providers measured agitation levels on a previously validated 6-point sedation scale at 0-, 5-, 10-, and 15-min after receiving sedation. We also assessed the incidence of adverse events, repeat or rescue medication dosing, and changes in vital signs.
Results: 106 patients were enrolled and 98 met eligibility criteria. There was no significant difference between groups in initial agitation scores. Based on agitation scores, more patients in the ketamine group were no longer agitated than the other medication groups at 5-, 10-, and 15-min after receiving medication. Patients receiving ketamine had similar rates of redosing, changes in vital signs, and adverse events to the other groups.
Conclusion: In highly agitated and violent emergency department patients, significantly fewer patients receiving ketamine as a first line sedating agent were agitated at 5-, 10-, and 15-min. Ketamine appears to be faster at controlling agitation than standard emergency department medications.

1. Introduction

1.1. Background

Emergency physicians often need to control violent, psychotic, or intoxicated patients who present a danger to themselves and hospital personnel. Rational reasoning, bargaining, shows of force with security guards, and even physical restraint are sometimes ineffective in controlling the acutely agitated patient. Chemical sedation is sometimes necessary to prevent injuries to patients and staff, and to allow safe medical evaluation and treatment. Benzodiazepines and typical antipsychotics such as haloperidol, the most commonly used sedative agents, have limitations including slow onset, respiratory depression, and variability in clinical response [1,2].

1.2. Importance

While several recent studies have shown the efficacy of ketamine for sedation in the prehospital setting [3,4] and as a rescue medication in emergency department (ED) patients who failed previous sedation attempts [5], there is limited data evaluating the effectiveness of ketamine as a first line agent for sedating agitated patients in the ED.

1.3. Goals of this investigation

The goal of our study was to compare the effectiveness and safety of ketamine to standard sedatives in agitated ED patients. Specifically, our primary objective was to compare the time to a defined reduction in agitation scores for ketamine versus benzodiazepines and haloperidol, alone or in combination. Our secondary objective was to assess the incidence of adverse events, repeat or rescue medication dosing, and changes in vital signs. We hypothesized that ketamine would produce the desired clinical effect in a shorter time, with similar side effects, stable hemodynamics, and less repeat dosing.

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Table 1
Study group demographics.

	Ketamine (n = 24)	Midazolam (n = 17)	Lorazepam (n = 33)	Haloperidol (n = 14)	Combo (n = 10)	p
Median age (range)	29 (19–58)	43 (18–51)	43 (20–63)	44 (21–58)	40.5 (21–58)	0.033
Male sex, no. (%)	19 (79.2%)	18 (94.7%)	19 (57.6%)	11 (78.6%)	9 (90.0%)	0.026
Race, no. (%)						
African American	3 (12.5%)	1 (5.3%)	5 (15.2%)	1 (7.1%)	1 (10.0%)	0.931
Asian	1 (4.3%)	0 (0.0%)	1 (3.1%)	1 (7.1%)	0 (0.0%)	
Hispanic	10 (41.7%)	10 (52.6%)	13 (39.4%)	8 (57.1%)	7 (70.0%)	
White	10 (43.5%)	7 (36.8%)	13 (40.6%)	4 (28.6%)	2 (20.0%)	
Drug use, no. (%)						
Yes	13 (54.2%)	12 (63.2%)	26 (78.8%)	12 (85.7%)	6 (60.0%)	0.168
No	11 (47.8%)	7 (36.8%)	7 (21.9%)	2 (14.3%)	4 (40.0%)	
Unknown						
Alcohol use, no. (%)						
Yes	8 (33.3%)	8 (42.1%)	8 (24.2%)	5 (35.7%)	2 (20.0%)	0.365
No	12 (52.2%)	7 (36.8%)	14 (21.9%)	5 (35.7%)	2 (20.0%)	
Unknown	4 (17.4%)	4 (21.1%)	11 (34.4%)	4 (28.6%)	6 (60.0%)	
Prior psychiatric visits, no. (%)						
Yes	7 (30.4%)	7 (36.8%)	17 (53.1%)	7 (50.0%)	5 (50.0%)	0.459

2. Methods

2.1. Study design

This was a single-center, prospective, observational study examining agitated ED patients requiring medication for sedation. IRB approval was obtained from our local institution.

2.2. Setting and participants

The study took place at a single urban level one trauma center ED with an annual census of 115,000 visits. A convenience sample was enrolled from May 2013 to January 2015.

Acutely agitated patients between the ages of 18 and 65 who required chemical sedation for acute agitation according to an emergency medicine resident or attending physician were eligible for enrollment. Pregnant women, prisoners and persons in police custody were excluded. Also excluded were those triaged to a low acuity zone of the ED that did not have continuous cardiorespiratory monitoring. Our study population included only those patients so severely agitated that they required care in a high acuity treatment area with available cardiorespiratory monitoring.

2.3. Variables

We initially defined four groups for comparison: ketamine, benzodiazepines, haloperidol, and a benzodiazepine plus haloperidol. Because the benzodiazepine group was comprised entirely of midazolam and lorazepam, we considered them separately, and compared a total of five groups. Due to the observational nature of this study, medication dosages were not uniform. Current published dosage recommendations for these medications include: ketamine 4–6 mg/kg intramuscular (IM) or 1–2 mg/kg intravenous (IV) [6-7], haloperidol 5–10 mg IM [8], midazolam 5–10 mg IM [9] or 5 mg IV[10], lorazepam 1–2 mg IV or IM [11].

2.4. Outcomes

Providers measured the patients' agitation on a previously validated 6-point sedation scale that was developed to monitor changes in agitation in ED patients [10,12]. In keeping with previous studies, adequate sedation was defined as an agitation score of ≤2 (see Appendix). Agitation was recorded by the treating physician prior to medication administration and at 5-, 10-, and 15-min after medication administration. Providers also recorded the time at which they thought adequate sedation had been achieved.

The incidence of adverse events, repeat or rescue medication dosing, and changes in vital signs were retrospectively abstracted from the electronic health record.

2.5. Measurement

ED physicians completed a structured data collection form (see Appendix). One trained author (AT) reviewed the relevant portion of each patient's medical record for the index visit and any return visits to our ED within 7 days. The abstractor was blinded to the study hypothesis until abstraction was complete. The abstractor received two 90-

Table 2
Study group dispositions.

	Ketamine	Midazolam	Lorazepam	Haloperidol	Combo	p
Disposition, no. (%)						
Hospital admission	14 (58.3%)	10 (52.6%)	15 (46.9%)	7 (50.0%)	3 (30.0%)	0.944
Psychiatric admission	8 (33.3%)	1 (5.3%)	2 (6.3%)	1 (7.1%)	1 (10.0%)	
Discharge home	2 (8.3%)	8 (42.1%)	15 (46.9%)	6 (42.9%)	6 (60.0%)	
Admission location, no. (%)						
Intensive care unit	7 (29.2%)	5 (26.3%)	2 (6.3%)	3 (21.4%)	1 (10.0%)	0.412
Stepdown unit	1 (4.2%)	3 (15.8%)	4 (12.5%)	2 (14.3%)	0 (0.0%)	
Telemetry floor	1 (4.2%)	0 (0.0%)	3 (9.4%)	1 (7.1%)	0 (0.0%)	
Unmonitored floor	5 (20.8%)	2 (10.5%)	6 (18.8%)	1 (7.1%)	1 (10.0%)	
LOS ED, minutes (SD)	332.7 (242.8)	402.5 (304.9)	356.2 (298.4)	301.1 (193.3)	388.6(394.4)	0.865
LOS ICU, hours (SD)	157.8 (131.3)	182.0 (91.2)	123.0 (−)	236 (137.2)	0.0	0.889
LOS Hosp[a]	105.6 (97.7)	140.3 (99.4)	96.5 (106.7)	110.8 (99.0)	95.0 (44.6)	0.899
48 h bounceback[b]	2 (8.3%)	2 (10.5%)	2 (6.1%)	1 (7.1%)	0 (0.0%)	0.062

[a] Hospital length of stay only if admitted.
[b] Return ED visit within 48 h only if discharged home from the ED.