KALMED: Ketamine for Acute Agitation in the Emergency Department

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To assess the **effectiveness** and **safety** of IM ketamine < 2.5 mg/kg (low) compared to ≥ 2.5 mg/kg (high) for acute agitation in the emergency department (ED)

Acute Agitation

- Acute agitation is a common in the ED with an estimated 2.6% of patients in the ED presenting agitated[1]
- Precipitating factors: metabolic or endocrine disturbances, infection, trauma, psychiatric issues, and substance abuse[2]
- Leads to additional risks: 72.4% of physician survey respondents were victims of workplace violence[3]
- Common sedative agents include benzodiazepines and antipsychotics which may have a slow onset of action and cause respiratory depression, QTc prolongation, and extrapyramidal reactions[4]

Ketamine

- Recommended as an option for sedation in the 2017 American College of Emergency Physicians Clinical Policy[4]
- MOA: Non-competitive N-methyl-D-amine antagonist with sedative, amnestic, and analgesic properties
- Dose: 1 to 6 mg/kg IM with a relatively quick onset and short duration of action[5]
- Adverse effects: Transient hypertension, tachycardia, hypersalivation, nausea/vomiting, laryngospasm, and hypoxia[6]

Literature Review

- Ketamine is an effective sedative with a more rapid onset compared to other agents used in the ED and prehospital[6-10]
- Majority of studies utilized a dose of 4 mg/kg IM, with a maximum dose of 500 mg[8-10]
- Utilizing a lower dose of 2mg/kg IM with a maximum dose of 200 mg may be effective for the treatment of acute agitation while avoiding potential adverse events[11,12]

Methodology

Design:
Single-center, retrospective, double-arm study

Groups:
Ketamine IM < 2.5 mg /kg compared to ≥ 2.5 mg/kg

Sample size:
98 patients to detect a 20% difference

Inclusion Criteria:
- ED presentation with acute agitation
- Administration of IM ketamine for acute agitation

Exclusion Criteria:
- Age < 18 years of age
- Concomitant sedative administration

1 Primary Endpoint:
- Resolution of agitation within 5-25 minutes of ketamine administration

2 Secondary Endpoints:
- Use of IM or IV rescue medications within 30 minutes of ketamine
- Incidence of adverse events related to ketamine administration

Results

	Low dose (n=35)	High dose (n=16)	P-Value
Age (yr), m (IQR)	36 (28-53)	52 (36-61)	0.06
Sex (male), n (%)	26 (74.3)	12 (75.0)	0.96
BMI, m (IQR)	25.8 (23.4-35.4)	23.7 (22-28.6)	0.11
Sedative 30 min. prior to ketamine, m (IQR)	10 (28.6)	20 (43.8)	0.29
Ketamine dose (mg), m (IQR)	120 (100-200)	200 (200-250)	<0.01
Ketamine dose (mg/kg), m (IQR)	1.8 (1.4-2.1)	3.0 (2.8-3.4)	<0.01
Resolved agitation within 5-25 min., n (%)	32 (91.4)	16 (100.0)	0.54
Agent administered after ketamine, n (%)	4 (16)	0 (0.0)	0.55
Resp. support, n (%)	6 (17.1)	3 (18.8)	0.89
Intubation, n (%)*	4 (11.4)	1 (6.3)	1.00
Dystonia, n (%)	0 (0.0)	1 (6.3)	0.31
Nausea/vomiting, n (%)	3 (8.6)	0 (0.0)	0.54

M: mean; IQR: interquartile range; resp: respiratory
*Reason for intubation: Low dose: refractory agitation x1, over sedation x 1, other cause > 3 hours later x2; High dose: subdural hematoma x1

Conclusion

- **Limitation:** Retrospective design, did not meet sample size, low IM ketamine dose in high dose group
- **Effectiveness:** No difference in resolution of agitation in low dose compared to high dose IM ketamine group (91.4% vs 100%; p=0.54)
- **Safety:** Non-significant increase in intubation in the low dose group compared to the high dose group (11.4% vs 6.3%; p=1.00). Additionally, the majority intubations (3/5) were unrelated to ketamine administration
- **Future directions:** Expand time frame for data collection to meet power and design a future prospective study to validate results

Disclosure

The authors have nothing to disclose concerning possible financial or personal relationships with commercial entities

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