KALMED: Ketamine for Acute Agitation in the Emergency Department

Lauren Stambolic, PharmD; Marc McDowell, PharmD, BCPS; Dharati Desai, PharmD, BCCCP; Jaxson Burkins, PharmD, BCPS; Nadine Lomotan, PharmD; Tasneem Ahmed, MD; Stephany Nuñez Cruz, PharmD, BCPS

Advocate Christ Medical Center Oak Lawn, IL

Background

- An estimated 2.6% of emergency department (ED) patients present with acute agitation1.
- Acute agitation can increase risk to staff as 72.4% of physician survey respondents reported violence in the workplace2.
- Common sedative agents include benzodiazepines and antipsychotics which may have a slow onset of action and cause respiratory depression, QTc prolongation, and extrapyramidal reactions3.
- Ketamine is an effective sedative with a more rapid onset compared to other agents used in the ED and prehospital setting4-6.

- Ketamine:
  - Recommended as a sedative option in the 2017 American College of Emergency Physicians Clinical Policy4.
  - MOA: Non-competitive N-methyl-D-amine antagonist with sedative, anesthetic, and analgesic properties.
  - Dose: 1 to 6 mg/kg IM with a relatively quick onset and short duration of action5.
  - Adverse effects: Transient hypertension, tachycardia, hypersalivation, nausea/vomiting, laryngospasm, and hypoxia6.
- Majority of studies utilized a dose of 4 mg/kg IM, with a maximum dose of 500 mg4-10.
- Utilizing a lower dose of 2 mg/kg IM with a maximum dose of 200 mg may be effective for the treatment of acute agitation while avoiding potential adverse events11-12.

Objective

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 ED.

Methodology

- Design: Single-center, retrospective, double-arm study.
- Groups:
  - Ketamine < 2.5 mg/kg compared to ≥ 2.5 mg/kg.
- Inclusion Criteria:
  - ED presentation with acute agitation
  - Administration of IM ketamine for acute agitation.
- Exclusion Criteria:
  - Age < 18 years of age
  - Concomitant sedative administration.

Methodology Continued

Sample Size:
98 patients to detect a 20% difference

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

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

Results

<table>
<thead>
<tr>
<th>Age (yr), m (IQR)</th>
<th>Low dose (n=35)</th>
<th>High dose (n=16)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (male), n (%)</td>
<td>36 (28-53)</td>
<td>52 (36-61)</td>
<td>0.06</td>
</tr>
<tr>
<td>BMI, m (IQR)</td>
<td>26 (74.3)</td>
<td>12 (75.0)</td>
<td>0.96</td>
</tr>
<tr>
<td>Ketamine dose mg/kg, m (IQR)</td>
<td>25.8 (23.4-35.4)</td>
<td>23.7 (22.8-28.6)</td>
<td>0.11</td>
</tr>
<tr>
<td>Sedative 30 min. prior to ketamine, n (%)</td>
<td>10 (28.6)</td>
<td>7 (43.8)</td>
<td>0.29</td>
</tr>
<tr>
<td>Ketamine dose mg/kg, m (IQR)</td>
<td>120 (100-200)</td>
<td>200 (200-250)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Ketamine dose mg/kg, m (IQR)</td>
<td>1.8 (1-4.2-1)</td>
<td>3.0 (2.8-3.4)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

| 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: median; IQR: interquartile range; resp: respiratory

*Reason for intubation: Low dose: over sedation x 1, refractory agitation > 1 hour later x 1, other cause > 3 hours later x 2; High dose: subdural hematoma x 1

Resolution of agitation within 5-25 minutes of ketamine administration

<table>
<thead>
<tr>
<th>&lt;2.5 mg/kg</th>
<th>&gt;2.5 mg/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>m (IQR)</td>
<td>m (IQR)</td>
</tr>
<tr>
<td>1.2 (0.4)</td>
<td>1.8 (0.6)</td>
</tr>
</tbody>
</table>

P-Value

- <0.01
- 0.06
- 0.96
- 0.11
- 0.29
- <0.01
- 0.54
- 0.55
- 0.89
- 1.00
- 0.31
- 0.54

Conclusion

- Limitations: 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); however, the majority intubations (4/5) 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.

Contact Information

Lauren.Stambolic@ahah.org

References