Impact of clinical guideline implementation of adult ketamine dosing in the emergency department

Julia Dickman PharmD
Impact of Clinical Guideline Implementation of Adult Ketamine Dosing in the Emergency Department

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Parkview Health

The speaker has no actual or potential conflict of interest in relation to this presentation.
Ketamine Indications

Food and Drug Administration (FDA) Labeled Indication

• Sedation

Off-Label Indications

• Analgesia
• Procedural sedation
• Excited delirium
• Status asthmaticus
Adverse Effects

- Hypertension
- Sedation
- Emergence Delirium
- Respiratory Depression
- Salivation

  - Mood Alteration
  - Dissociation
  - Vivid Dreams
  - Hallucinations
Factors Influencing Adverse Events

- Varying Routes
- Multiple Strength Vials
- Varying Doses
- Rate of Administration

Inappropriate Dosing

Adverse Effects
## Ketamine Dosing

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dose</th>
<th>Subdissociative or Dissociative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid Sequence Intubation (RSI)</td>
<td>1 – 4.5 mg/kg Intravenous (IV)</td>
<td>Dissociative</td>
</tr>
<tr>
<td></td>
<td>4 – 13 mg/kg Intramuscular (IM)</td>
<td></td>
</tr>
<tr>
<td>Procedural Sedation</td>
<td>1 – 2 mg/kg IV</td>
<td>Dissociative</td>
</tr>
<tr>
<td></td>
<td>4 – 5 mg/kg IM</td>
<td></td>
</tr>
<tr>
<td>Pain</td>
<td>0.2 – 0.8 mg/kg IV</td>
<td>Subdissociative</td>
</tr>
<tr>
<td></td>
<td>0.5 – 1 mg/kg Intranasal (IN)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.5 mg/kg Oral (PO)</td>
<td></td>
</tr>
<tr>
<td>Agitated Delirium</td>
<td>4 – 6 mg/kg IM</td>
<td>Dissociative</td>
</tr>
<tr>
<td></td>
<td>1 – 2 mg/kg IV</td>
<td></td>
</tr>
<tr>
<td>Status Asthmaticus</td>
<td>1 – 2 mg/kg IV</td>
<td>Dissociative</td>
</tr>
</tbody>
</table>
Test Your Knowledge

- Subdissociative dosing of ketamine is utilized for which off-label indication?
  a) Pain
  b) Procedural sedation
  c) Rapid sequence intubation
  d) Agitated delirium
Test Your Knowledge

- Sub dissociative dosing of ketamine is utilized for which off-label indication?
  
  a) Pain  
  b) Procedural sedation  
  c) Rapid sequence intubation  
  d) Agitated delirium
Test Your Knowledge

• What is the most appropriate dose of ketamine for status asthmaticus?

  a) 5 mg/kg IM
  b) 1 mg/kg IV push
  c) 0.3 mg/kg IV push
  d) 2 mg/kg PO
Test Your Knowledge

• What is the most appropriate dose of ketamine for status asthmaticus?
  a) 5 mg/kg IM
  b) 1 mg/kg IV push
  c) 0.3 mg/kg IV push
  d) 2 mg/kg PO
Baird, et al.

- Intervention: Emergency Department (ED) adult ketamine order panel
- Indications
  - RSI
  - Procedural sedation
  - Pain
- Pre-Post Study
- Primary Outcome: Appropriate Dose
  - OR = 2.94, 95% confidence interval (1.1-7.8), p = 0.0231

Hospital Pharmacy. 2017;52(7)483:7.
Parkview Health
Purpose

• Following the implementation of an ED adult ketamine order set, evaluate:
  • Appropriateness of ketamine dosing
  • Patient outcomes
  • Adverse events

• Demonstrate benefit of pharmacy-driven education
**Objectives**

<table>
<thead>
<tr>
<th>Primary Objective</th>
<th>Secondary Objectives</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Evaluate appropriateness of ketamine dose for indication</td>
<td></td>
</tr>
<tr>
<td>• Before and after order set implementation</td>
<td>• Describe adverse events</td>
</tr>
<tr>
<td></td>
<td>• Assess impact of pharmacy-driven education on comfort level for</td>
</tr>
<tr>
<td></td>
<td>• Physicians</td>
</tr>
<tr>
<td></td>
<td>• Pharmacists</td>
</tr>
<tr>
<td></td>
<td>• Nurses</td>
</tr>
</tbody>
</table>
Study Design and Statistical Analysis

Study Design
- Institution Review Board Approved
- Multicenter
- Retrospective
- Pre-Post Intervention
- Cohort Study

Statistical Analysis
- Primary Outcome
  - Mann-Whitney U Test
- Secondary Outcomes
  - Adverse Effects
    - Wilcoxon Signed Rank
  - Survey Data
    - Mann-Whitney U Test
Inclusion and Exclusion Criteria

### Inclusion Criteria
- Patients $\geq$ 18 years old
- Presenting to the ED at any Parkview Hospital
- Receiving $\geq$ 1 dose of ketamine
  - Intravenous (IV) push
  - Intramuscular (IM)
  - Intranasal (IN)

### Exclusion Criteria
- Pregnant
- Continuous IV infusion
- Pre-hospital ketamine administration
ED Adult Ketamine Order Set

**RSI**
- 1 - 2 mg/kg IV push once

**Procedural Sedation**
- 0.5 – 2 mg/kg IV push once, may repeat x1 q10min
- 1 – 3 mg/kg IM once, may repeat x1 q10min

**Pain Management**
- 0.3 mg/kg IV push once, may repeat x1 q20min
- Admin Comments: max single dose = 30mg, dilute to 10ml with NS

**Intranasal Ketamine for Pain**
- 1 mg/kg intranasal (IN) once

**Agitated Delirium**
- 5 mg/kg IM once, may repeat x1 q10min

**Status Asthmaticus**
- 1 mg/kg IV push, may repeat x1 q10min
Survey Questions

Physician
- Familiarity with ketamine dosing
- Comfort level dosing ketamine
- Likelihood of ordering ketamine

Pharmacist
- Familiarity with ketamine dosing
- Comfort level verifying ketamine orders

Nursing
- Comfort level administering ketamine
- Comfort level monitoring patients after administration of ketamine
Protocol Timeline

July – November 2018
Pre-Implementation

February 2019
Implementation of Ketamine Order Set

March 2019
Post-Implementation

Early February 2019
Pre-Survey Provided

Late February 2019
Education and Post-Survey Provided
PATIENT RESULTS
Study Population

Pre-Order Set Implementation

- 255 Ketamine Patients Screened
- 167 Patients Excluded
  - 122 Pediatric Patients
  - 43 Missing Data
  - 2 Prior Ketamine Use
- 88 Ketamine Patients

Post-Order Set Implementation

- 38 Ketamine Patients Screened
- 26 Patients Excluded
  - 15 Pediatric Patients
  - 11 Missing Data
- 12 Ketamine Patients
## Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Pre-Implementation (n = 88)</th>
<th>Post-Implementation (n = 12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender, male [n (%)]</td>
<td>47 (53)</td>
<td>7 (58)</td>
</tr>
<tr>
<td>Age, years [median (IQR)]</td>
<td>51 (34 – 66)</td>
<td>60 (48 – 69)</td>
</tr>
<tr>
<td>Weight, kilograms [median (IQR)]</td>
<td>82 (65 – 100)</td>
<td>75 (70 – 98)</td>
</tr>
<tr>
<td>Psychiatric Comorbidity [n (%)]</td>
<td>5 (6)</td>
<td>1 (8)</td>
</tr>
<tr>
<td>Drug Abuse [n (%)]</td>
<td>6 (7)</td>
<td>4 (33)</td>
</tr>
</tbody>
</table>
Ketamine Use by Facility

Ketamine Use Prior to Implementation (n = 88)

- Parkview Regional Medical Center: 44%
- Parkview Randallia Hospital: 29%
- Parkview Warsaw: 17%
- Community Hospitals: 10%

Ketamine Use After Implementation (n = 12)

- Parkview Regional Medical Center: 50%
- Parkview Randallia Hospital: 25%
- Parkview Warsaw: 8%
- Community Hospitals: 17%
Ketamine Use by Indication

**Ketamine Use Prior to Implementation**  
(n = 88)

- **Procedural Sedation**: 57%
- **RSI**: 26%
- **Pain**: 17%

**Ketamine Use After Implementation**  
(n = 12)

- **Procedural Sedation**: 42%
- **RSI**: 50%
- **Status Asthmaticus**: 8%
## Results – Primary Outcome
### Percent Appropriate by Indication

<table>
<thead>
<tr>
<th>Indication (Reference Range)</th>
<th>Pre-Implementation</th>
<th>Post-Implementation</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedural Sedation (IV: 0.5 – 2 mg/kg IM: 1 – 3 mg/kg)</td>
<td>47</td>
<td>27 (57)</td>
<td>5</td>
</tr>
<tr>
<td>RSI (IV: 1 – 2 mg/kg)</td>
<td>26</td>
<td>21 (81)</td>
<td>5</td>
</tr>
<tr>
<td>Pain (IV: 0.3 mg/kg IN: 1 mg/kg)</td>
<td>15</td>
<td>12 (80)</td>
<td>1</td>
</tr>
<tr>
<td>Status Asthmaticus (IV: 1 mg/kg)</td>
<td>0</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Overall</td>
<td>88</td>
<td>60 (68)</td>
<td>12</td>
</tr>
</tbody>
</table>
## Results – Secondary Outcome

<table>
<thead>
<tr>
<th></th>
<th>Pre-Implementation [Median (IQR)] (n = 88)</th>
<th>Post-Implementation [Median (IQR)] (n = 12)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-Ketamine SBP</td>
<td>126 (108 – 148)</td>
<td>132 (111 – 140)</td>
<td>0.9239</td>
</tr>
<tr>
<td>Post-Ketamine SBP</td>
<td>134 (112 – 158)</td>
<td>124 (112 – 140)</td>
<td>0.5885</td>
</tr>
<tr>
<td>Pre-Ketamine Pulse, BPM</td>
<td>92 (75 – 107)</td>
<td>96 (80 – 104)</td>
<td>0.7583</td>
</tr>
<tr>
<td>Post-Ketamine Pulse, BPM</td>
<td>90 (78 – 108)</td>
<td>99 (88 – 113)</td>
<td>0.2453</td>
</tr>
</tbody>
</table>

SBP: Systolic blood pressure (reported in mmHg)
BPM: Beats per minute
# Results – Secondary Outcome

<table>
<thead>
<tr>
<th></th>
<th>Pre-Implementation [Median (IQR)] (n = 88)</th>
<th>Post-Implementation [Median (IQR)] (n = 12)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-Ketamine RR</td>
<td>20 (16 – 24)</td>
<td>19 (17 – 22)</td>
<td>0.8234</td>
</tr>
<tr>
<td>Post-Ketamine RR</td>
<td>18 (15 – 23)</td>
<td>21 (18 – 25)</td>
<td>0.1024</td>
</tr>
<tr>
<td>Pre-Ketamine O2 Saturation, %</td>
<td>98 (96 – 100)</td>
<td>99 (94 – 100)</td>
<td>0.8345</td>
</tr>
<tr>
<td>Post-Ketamine O2 Saturation, %</td>
<td>99 (96 – 100)</td>
<td>98 (95 – 100)</td>
<td>0.5435</td>
</tr>
</tbody>
</table>

RR: respiratory rate, reported in breaths per minute
O2: oxygen

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# Results – Secondary Outcome

<table>
<thead>
<tr>
<th>O2 Intervention (n, %)</th>
<th>Pre-Implementation (n = 88)</th>
<th>Post-Implementation (n = 12)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasal cannula</td>
<td>16 (18)</td>
<td>3 (25)</td>
<td>0.5741</td>
</tr>
<tr>
<td>Unplanned Intubation</td>
<td>2 (2)</td>
<td>1 (8)</td>
<td>0.2507</td>
</tr>
<tr>
<td>Bag valve mask</td>
<td>1 (1)</td>
<td>0 (0)</td>
<td>0.7119</td>
</tr>
</tbody>
</table>
## Results – Secondary Outcome

<table>
<thead>
<tr>
<th></th>
<th>Pre-Implementation</th>
<th>Post-Implementation</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>GCS [Median (IQR)]</td>
<td>N</td>
</tr>
<tr>
<td>Pre-Ketamine GCS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Intubated</td>
<td>59</td>
<td>15 (15 – 15)</td>
<td>5</td>
</tr>
<tr>
<td>Post-Ketamine GCS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Intubated</td>
<td>59</td>
<td>13 (8 – 15)</td>
<td>5</td>
</tr>
<tr>
<td>Pre-Ketamine GCS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intubated</td>
<td>29</td>
<td>15 (3 – 15)</td>
<td>7</td>
</tr>
<tr>
<td>Post-Ketamine GCS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intubated</td>
<td>29</td>
<td>3 (3 – 8)</td>
<td>7</td>
</tr>
</tbody>
</table>

GCS: Glasgow Coma Scale
## Results – Secondary Outcome

<table>
<thead>
<tr>
<th></th>
<th>Pre-Implementation [n (%)] (n = 88)</th>
<th>Post-Implementation [n (%)] (n = 12)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzodiazepine Use</td>
<td>1 (1)</td>
<td>0 (0)</td>
<td>0.7119</td>
</tr>
<tr>
<td>Atropine Use</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>-</td>
</tr>
<tr>
<td>Glycopyrrolate Use</td>
<td>9 (10)</td>
<td>0 (0)</td>
<td>0.2479</td>
</tr>
</tbody>
</table>
SURVEY RESULTS
Physician Familiarity with Ketamine Dosing

Pre-Education

Post-Education

\( p = 0.0076 \)
Physician Comfort with Ketamine Dosing

Pre-Education

- Pain
- RSI
- Procedural Sedation
- Agitated Delirium
- Status Asthmaticus*
- Intranasal Pain*

Post-Education

- Pain
- RSI
- Procedural Sedation
- Agitated Delirium
- Status Asthmaticus*
- Intranasal Pain*

p = 0.0212
p = 0.0178
Physician Likelihood of Ordering Ketamine

Pre-Education

- Pain*
- Agitated Delirium*
- Status Asthmaticus*
- Intranasal Pain*

Not at all Familiar
- Extremely Familiar
- Very Familiar
- Somewhat Familiar
- Not so Familiar
- Not at all Familiar

Post-Education

- Pain*
- Agitated Delirium*
- Status Asthmaticus*
- Intranasal Pain*

Not at all Familiar
- Extremely Familiar
- Very Familiar
- Somewhat Familiar
- Not so Familiar
- Not at all Familiar

p = 0.0185
p = 0.0375
p = 0.0155
p = 0.0194
Pharmacist Familiarity with Ketamine Dosing

Pre-Education

Post-Education

- Pain
- RSI
- Procedural Sedation
- Agitated Delirium
- Status Asthmaticus
- Intranasal Pain

Extremely Familiar
Very Familiar
Somewhat Familiar
Not so Familiar
Not at all Familiar

Comparison of familiarity levels before and after education.
Pharmacist Comfort Level with Verifying Ketamine Orders

Pre-Education

Post-Education
Nursing Comfort Level Administering Ketamine

Pre-Education

- Pain
- RSI
- Procedural Sedation
- Agitated Delirium
- Status Asthmaticus
- Intranasal Pain

Post-Education

- Pain
- RSI
- Procedural Sedation
- Agitated Delirium
- Status Asthmaticus
- Intranasal Pain

Extremely Familiar | Very Familiar | Somewhat Familiar | Not so Familiar | Not at all Familiar

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Nursing Comfort Level Monitoring

Patients

Pre-Education

- Pain
- RSI
- Procedural Sedation
- Agitated Delirium
- Status Asthmaticus
- Intranasal Pain

Post-Education

- Pain
- RSI
- Procedural Sedation
- Agitated Delirium
- Status Asthmaticus
- Intranasal Pain

Legend:
- Extremely Familiar
- Very Familiar
- Somewhat Familiar
- Not so Familiar
- Not at all Familiar
Discussion

• Most common indications
  • RSI
  • Procedural Sedation

• Multiple doses
  • Failure to respond vs. continued sedation

• Limited use of order set
  • Recent implementation
  • Acuity of situation

• Low rates of adverse effects
  • Low GCS → intubated patients

• Use in schizophrenia
Conclusions

• Trend towards increased appropriate doses
• No clinically relevant differences in adverse effects
• Education increased familiarity, comfort level, and likelihood of ordering ketamine
Limitations

• Retrospective nature
• Small sample size
• Underpowered
• Post-order set sample includes patients who did not have ketamine ordered from the order set
• Acuity of patients
• Timeline
Future Direction

- Discuss incorporating into nursing quick orders
- Encourage utilization of ketamine order set
- Creation of pediatric ketamine order set
Acknowledgements

• Sarah E. Meeks, PharmD
• Kassandra A. Foellinger, PharmD, BCPS
• Sarah Ferrell, PharmD
References

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