Low-dose Ketamine for Prehospital Analgesia
Stephanie Wuerffel, PharmD, PGY-1 Pharmacy Resident, Bozeman Health Deaconess Hospital

**Background**

**Ketamine Pharmacology and Low-Dose Ketamine Analgesia**
- Non-competitive NMDA receptor antagonist
- Enhances DA activity, α- and β- agonist activity
- Augments the action of opioids at C-fiber synapses
- Doses ≤0.5 mg/kg for analgesia ("sub-dissociative" doses)
  - Rarely cause significant adverse effects
  - SE easily treatable with low-dose benzodiazepines
- Analgesia onset: 30 sec & duration: 20-45 min
- Advantages of low-dose ketamine analgesia vs. opioids
  - Increased BP & HR, less adverse respiratory effects
- Synergistic analgesia of ketamine with opioids
- Adverse effects of ketamine
  - Psychological effects
  - Nausea, vomiting, elevated BP and HR
  - Bronchodilation, hypersalivation, laryngospasm
  - Serious side effects rare with low doses

**Prehospital Ketamine Analgesia**
- Ketamine administration by trained, non-physician responders is safe and effective
  - Based on large, prospective studies
- Ketamine has been widely-adopted for prehospital use
  - UK, Australia & rural, limited-resource countries
  - US military, backcountry/wilderness EMS
- Prehospital ketamine analgesia in Gallatin Valley, MT
  - Potentially useful for AMR Bozeman operation
  - Prolonged extrications and transport durations
  - Traumatic injury common
  - Often related to outdoor recreation

**American Medical Response Bozeman**
- Emergency & non-emergency medical transport service
  - Approximately 42 paramedics and EMTs
- Annual average ~3,600 calls
- Serves the Gallatin County area

**MT Prehospital Treatment Protocol Ketamine Restrictions**
- Only for analgesia at low, sub-dissociative doses
  - 0.1-0.5 mg/kg
  - IV administration only
  - SBP > 100 mmHg required for use

**Methods**

**Study Objectives**
- Implement a safe and effective process for AMR Bozeman to use low-dose ketamine for analgesia
- Evaluate pain before and after ketamine administration
- Evaluate adverse effects after ketamine administration
- Assess the paramedics’ level of satisfaction, opinions, and concerns with low-dose ketamine analgesia

**Study Design and Protocols**
- Prospective, observational study
  - Pilot study for low-dose, prehospital ketamine use
- Prehospital protocol for ketamine analgesia
  - Developed by pharmacists and AMR Bozeman
  - Designed to match existing MT state EMS protocols
- Pharmacist-developed field protocol
  - Copy posted inside of every ambulance
  - See “Ketamine Field Protocol” for protocol details

**Ketamine Education**
- Mandatory pharmacist-led education for paramedics
  - Focus on prehospital ketamine use for analgesia

**Data Collection and Analysis**
- Pilot study planned for 11/1/2015 - 4/30/2016
  - Data collection from AMR’s EMR throughout study period
  - Will also collect subjective input from patients and EMS staff
  - Statistical analysis of pain score changes through MSU

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**Ketamine Field Protocol**

**Indications:** Patients >5 years old with pain of traumatic origin or opioid refractory pain; Opioid-tolerant patients >5 years old with an acute exacerbation of pain

**Contraindications:** Hypersensitivity to ketamine, chest pain of suspected cardiac origin, any condition in which hypertension could lead to complications (ex. hypertensive crisis, amphetamine abuse), psychiatric problems (relative), SBP <100

**Ketamine Dosing Chart**

<table>
<thead>
<tr>
<th>Kg</th>
<th>20</th>
<th>30</th>
<th>40</th>
<th>50</th>
<th>60</th>
<th>70</th>
<th>80</th>
<th>90</th>
<th>≥100</th>
</tr>
</thead>
<tbody>
<tr>
<td>mg</td>
<td>4</td>
<td>6</td>
<td>8</td>
<td>10</td>
<td>12</td>
<td>14</td>
<td>16</td>
<td>18</td>
<td>20</td>
</tr>
<tr>
<td>mL</td>
<td>0.4</td>
<td>0.6</td>
<td>0.8</td>
<td>1</td>
<td>1.2</td>
<td>1.4</td>
<td>1.6</td>
<td>1.8</td>
<td>2</td>
</tr>
</tbody>
</table>

**Administration:** Give slow IV push over 60 seconds. May repeat x1 only with online medical control

**Monitoring:** Blood pressure, heart rate, SpO₂, mental status, pain rating (before & after ketamine, upon ED admission), ECG

**Mediating Adverse Effects:** Agitation or aggression: ≥12 years old: Midazolam 1mg IV, <12 years old: Midazolam 0.5mg IV, repeat doses PRN; Laryngospasm: Bag-valve-mask assembly and airway maneuvers; Hypersalivation: Atropine 0.5 mg IV
### Preliminary Results

#### Patient and Run Information

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean</th>
<th>Median</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Age (years)</td>
<td>38.8</td>
<td>32</td>
<td>14 - 84</td>
</tr>
<tr>
<td>Patient Weight (kg)</td>
<td>78</td>
<td>60</td>
<td>54 - 113</td>
</tr>
<tr>
<td>Total distance (miles)</td>
<td>11.9</td>
<td>13.2</td>
<td>2.7 - 23.2</td>
</tr>
<tr>
<td>Duration (minutes)</td>
<td>71.6</td>
<td>67.5</td>
<td>31 - 196</td>
</tr>
</tbody>
</table>

#### Parameter | Patients (n=15) | %
---|---|---
Male | 9 | 60%
Morphine + Ketamine | 4 | 26.7%
Fentanyl + Ketamine | 6 | 40%

#### Indication for Ketamine

| Indication | Patients (n=15) | %
---|---|---
Pain of traumatic origin | 5 | 33.3%
No/poor response to opioids and pain of traumatic origin | 7 | 46.7%
No/poor response to opioids | 1 | 6.7%
Chronic pain exacerbation | 1 | 6.7%
Both refused opioids and pain of traumatic origin | 1 | 6.7%

#### Ketamine Protocol Compliance

- 3 patients received ketamine off-protocol
  - 1 unintentional – 10x protocol dose (1st study patient)
  - 2 intentional – 1 used IM, 1 low-dose per patient

#### Ketamine Pain Score Results

<table>
<thead>
<tr>
<th>Pain Score Change with Ketamine</th>
<th>Mean</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>All ketamine patients</td>
<td>-3.25</td>
<td>-3</td>
</tr>
<tr>
<td>Ketamine per protocol</td>
<td>-3.5</td>
<td>-3.5</td>
</tr>
</tbody>
</table>

#### Ketamine Results and Adverse Effects

| Result or ADR | Patients (n=15) | %
---|---|---
"Improved" | 12 | 80%
"Unresolved" | 2 | 13.3%
"Deteriorated"* | 1 | 6.7%
No ADR | 12 | 80%
Dizziness | 1 | 6.7%
Dysphoria | 1 | 6.7%
Dissociation* | 1 | 6.7%

* 10x protocol dose given

#### Hemodynamic and Respiratory Changes

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>BP change after ketamine</td>
<td>+6.2 mmHg</td>
<td>+6 mmHg</td>
</tr>
<tr>
<td>Time (administration to BP)</td>
<td>21 minutes</td>
<td>19 minutes</td>
</tr>
</tbody>
</table>

- No notable trends with HR, RR, or SpO₂ and ketamine

### Preliminary Conclusions

#### Overall Experience and Future Directions

- Positive overall experience with ketamine analgesia
  - Seems to be safe and effective for analgesia
    - 10x OD with no severe cardiopulmonary sequelae
    - Seems to be a mild increase in BP at low doses
  - Patient satisfaction/response generally good
    - Dizziness occurred in 1 patient
    - Dysphoria occurred in 1 patient
    - Midazolam has not yet been used to mediate ADRs
  - AMR Bozeman will likely make ketamine a permanent option for analgesia in the field
    - Reevaluate ketamine protocol based on results
    - Indications, contraindications, dosing, monitoring
  - Respond to any future MT prehospital protocol changes
    - Eliminate/change minimum SBP for ketamine
    - Expansion of indications, routes, doses

### Contact Information

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### References