**Intranasal ketamine for abortive migraine therapy in pediatric patients: a case series**

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**BACKGROUND**

Migraine is a common presentation in adolescents and children in emergency departments (EDs) and inpatient visits. It is often treated with nonsteroidal anti-inflammatory drugs, dopamine receptor antagonists, triptans, or dihydroergotamine (DHE). Some cases, however, are refractory to traditional medications and options become narrowed. Restricting therapy further, DHE is currently on indefinite shortage. Ketamine, a lipophilic, rapid-acting, N-methyl-D-aspartate (NMDA) antagonist, has emerged as a promising therapeutic option. Excitatory glutamate signaling may be inhibited by ketamine via NMDA antagonism. This action could suppress cortical spreading depression (CSD) and alleviate migraines with and without aura.

Reports in mixed migraine patient populations described statistically significant pain score reductions (7.1 to 3.8; p<0.0001) with intermittent intravenous ketamine and diminished severity with ketamine infusions (0.12-0.42 mg/kg/hour) without serious adverse effects (AEs). Intranasal (IN) ketamine 25 mg in migraine patients with prolonged aura demonstrated statistically significant reduced aura severity (p=0.032). Reports of efficacy and safety with IN ketamine (0.3-0.5 mg/kg/dose) in pediatric patients with various pain diagnoses have been published, but pediatric migraine data with IN ketamine is lacking.

**OBJECTIVE**

Report efficacy and safety of IN ketamine in pediatric patients with refractory migraine.

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**METHODS**

- **Inclusion**
  - Pediatric patient (< 18 years old)
  - Presenting to CCIM ED or inpatient
  - Pain or Neurology Services deem patient refractory

- **Exclusion**
  - Intranasal ketamine
  - 0.1-0.2 mg/kg/dose (maximum 25 mg/dose)
  - Administered every 15 minutes (maximum of 5 doses)

- **Monitoring**
  - Numeric pain scores
  - Vital signs during and 1 hour post administration
  - Patient reported side effects (if stated)
  - Inpatient admissions and readmissions < 72 hours

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**RESULTS (continued)**

**Adverse Reactions**

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Responders (n=7)</th>
<th>Non-Responders (n=4)</th>
<th>Total (n=11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperemesis (nausea)</td>
<td>4 (57.14)</td>
<td>0</td>
<td>4 (57.14)</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>4 (57.14)</td>
<td>1 (25)</td>
<td>5 (38.46)</td>
</tr>
<tr>
<td>Tachypnea (nausea)</td>
<td>2 (28.57)</td>
<td>0</td>
<td>2 (28.57)</td>
</tr>
<tr>
<td>Nausea</td>
<td>1 (14.29)</td>
<td>0</td>
<td>1 (9.09)</td>
</tr>
<tr>
<td>Flashing</td>
<td>1 (14.29)</td>
<td>0</td>
<td>1 (9.09)</td>
</tr>
</tbody>
</table>

**Comorbid Diagnoses by Patient Response to IN Ketamine**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Responders (n=7)</th>
<th>Non-Responders (n=4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety disorder</td>
<td>4 (57.14)</td>
<td>0</td>
</tr>
<tr>
<td>Brain structure abnormality</td>
<td>3 (42.86)</td>
<td>0</td>
</tr>
<tr>
<td>Concomitant disorder</td>
<td>4 (57.14)</td>
<td>0</td>
</tr>
<tr>
<td>Depression</td>
<td>2 (28.57)</td>
<td>0</td>
</tr>
<tr>
<td>History of trauma</td>
<td>3 (42.86)</td>
<td>0</td>
</tr>
<tr>
<td>Head Traumatic Stress Disorder</td>
<td>1 (14.29)</td>
<td>0</td>
</tr>
<tr>
<td>Other (i.e. ADHD, autistic personality disorder, myalgia, panic disorder, inguinal neovascular)</td>
<td>1 (14.29)</td>
<td>0</td>
</tr>
</tbody>
</table>

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**STRENGTHS AND LIMITATIONS**

**STRENGTHS**

- First report utilizing IN ketamine in pediatric patients for migraine
- Easy and safe administration and monitoring

**LIMITATIONS**

- Retrospective in nature
- Small sample size
- No set study protocol to precisely analyze a specific regimen
- Difficult to discern if some adverse reactions (i.e. vital signs) are due to pain or medication

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**CONCLUSIONS**

Intranasal ketamine appears to be safe and effective for pediatric migraine treatment, particularly in patients with prolonged migraine. Patients with significant comorbidities did not respond as well and it is likely that patients who had an identifiable cause for their headache did not have true migraine. Our experience supports efficacy with lower IN ketamine doses (0.1-0.2 mg/kg/dose in repeated doses) in abortive migraine therapy with minimal AEs. Larger trials are warranted to substantiate ketamine’s efficacy, optimal dose, and safety for abortive migraine therapy in pediatric patients.

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**REFERENCES**