**Valproic Acid for Acute Migraine Critically Appraised Topic (CAT)**

**PICOT Question:**
In the pediatric patient diagnosed with acute migraine is valproic acid an effective treatment?; In the pediatric patient diagnosed with acute migraine is valproic acid an effective treatment compared to dihydroergotamine (DHE)?

**Clinical bottom line based on literature appraisal below:**
Valproic acid (VPA) may be an effective tool in the treatment of pediatric migraine (Edwards, Norton & Behnke, 2001; Reiter, Nickisch & Merritt, 2005). However, due to a limitation of established pediatric evidence, VPA must be considered a second-line pharmaceutical option at this time after failure of more established options like prochlorperazine (Migraine CPG Team; Consensus Opinion). The dose of VPA is 20mg/kg with a maximum of 1 gram (Gunn & Nechyba, 2002).

*GRADE = Strong recommendation / Low-quality evidence*

**Search strategy implemented:**

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**Search outcome:**
4 studies were identified, 2 addressed use of valproic acid for migraine prophylaxis. The remaining 2 articles are summarized below.

**Synthesis of relevant studies:**

<table>
<thead>
<tr>
<th>Author, date, country, and industry of funding</th>
<th>Patient Group</th>
<th>Level of Evidence (Oxford) / Strength of Evidence (GRADE)</th>
<th>Research design</th>
<th>Significant results</th>
<th>Limitations</th>
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<tbody>
<tr>
<td>Edwards, K.R., Norton, J., Behnke, M. (2001). Comparison of intravenous valproate versus intramuscular dihydroergotamine and metoclopramide for acute treatment of migraine headache. <em>Headache, 41</em>, 976-980.</td>
<td>Patients (N=40) with an International Headache Society (IHS) defined acute migraine (14 – 74 yoa) with or without aura</td>
<td>Oxford: 2b GRADE: weak recommendation to use VPA</td>
<td>Randomized Control Trial</td>
<td>No dropouts were identified. Headache severity (0-3 scale, 0=no headache, 1=mild, 2=moderate, 3=severe) and associated symptomatology (photophobia, phonophobia, and/or nausea) were rated at baseline, and 15, 30, 45 minutes and 1, 2, 4, and 24 hours. The researchers included the 24 hour time point from the analysis but did not believe it to accurately reflected the effects of the treatment.</td>
<td>Randomization process was not detailed. Power analysis and confidence intervals were not presented. Small study group population.</td>
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10 mg. followed by IM DHE (Dihydroergotamine) 1 mg. (n=20) in an alternating fashion. Patients receiving a triptan within 12 hours of presenting to the clinic were excluded from the study.

It did not appear there was any significant different between the two interventions:
- presence of a moderate-to severe headache at four hours was \( p = 0.36 \);
- nausea \( p = 0.26 \);
- photophobia \( p = 0.53 \);
- phonophobia \( p = 0.76 \).

The recurrence of migraine headache pain and symptomatology at 24 hours was higher in the VPA group than the DHE/MCLP group however a \( p \) value was not reported.


| Reiter, P.D., Nickisch, J., & Merritt, G. (2005) Efficacy and tolerability of intravenous valproic acid in acute adolescent migraine. Headache. 45, 899-903. | 31 charts were reviewed. 58 clinic visits and 78 valproic acid (VPA) infusions. Mean age was 15+/-2 years. 81% were female. Most received concomitant IV dexamethasone and or ondansetron. | No ranking available | Retrospective chart review | Intravenous VPA infusion did not make symptoms worse | Missing data pain scores and vital signs. Some patients received concomitant infusions of dexamethasone or ondansetron. |

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**Clinical bottom line authored by:** Migraine CPG Team

**Date created:**
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**References:**
