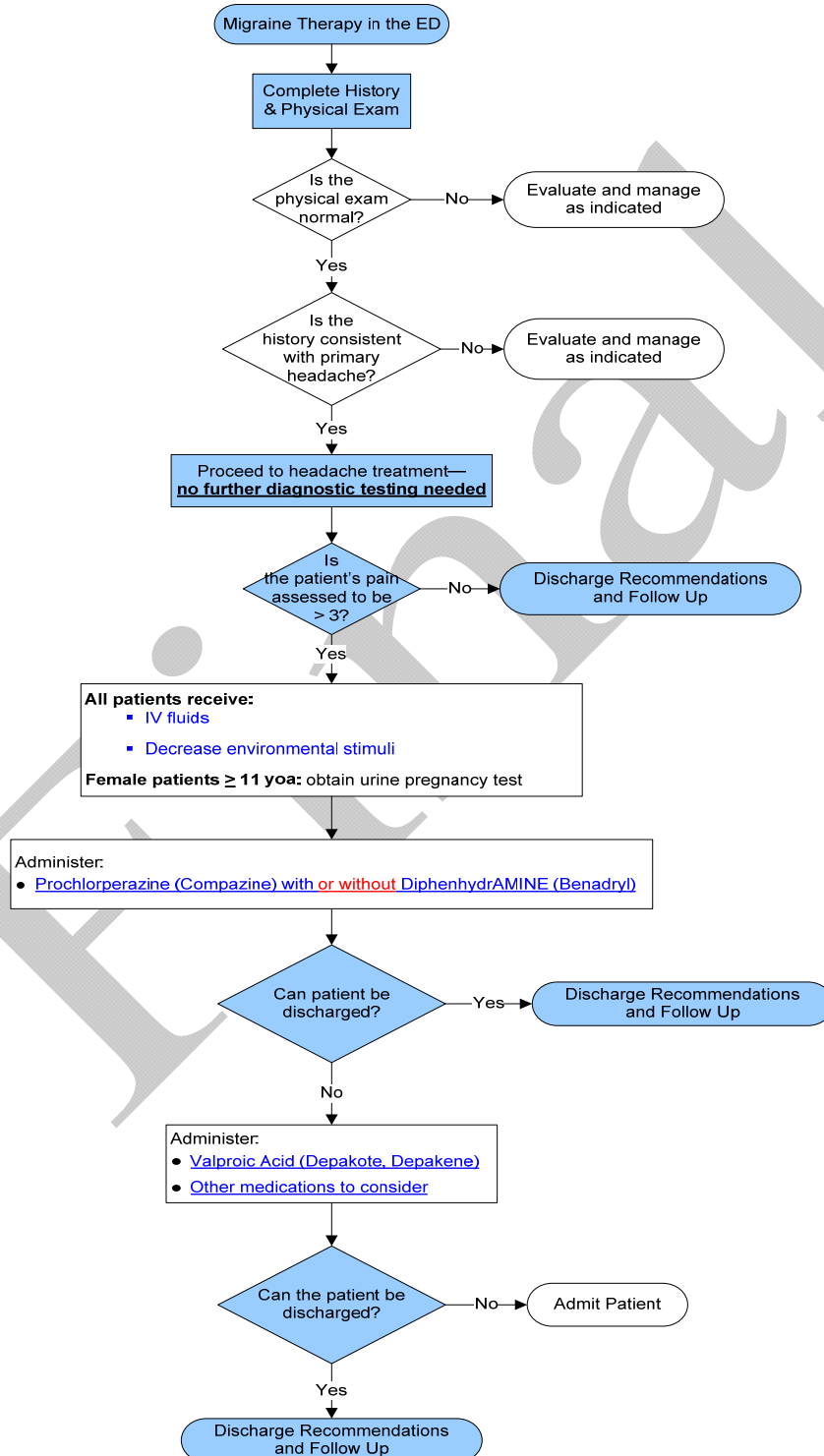


Children's Mercy Hospitals and Clinics
Evidence Based Practice Clinical Practice Guideline

Migraine CPG Synopsis



Epidemiology:

Migraine headaches are a common complaint in children. The frequency of migraine occurrence increases through adolescent. The prevalence of migraines increases with age:

- children age 3 – 7 years of age the migraine prevalence is 3%
- children 4 – 11 years of age it is reported to be 4 – 11%
- children 11 – 15 years of age the prevalence is reported to be 8 – 23% (Lewis, et al., 2004).

The mean age onset of migraines is 7.2 years for males and 10.9 for females (Lewis, et al.).

The patient with a refractory headache will typically present with:

- Headache attack lasting 1 to 72 hours
- Headache has at least 2 of the following 4 features:
 1. Either bilateral or unilateral (frontal/temporal) location
 2. Pulsating quality
 3. Moderate to severe intensity
 4. Aggravated by routine physical activities
- At least 1 of the following accompanies headache:
 1. Nausea and/or vomiting
 2. Photophobia and phonophobia (may be inferred from their behavior) (Lewis et al., 2004).

Objective of Guideline: To standardize the care of children seen in the Emergency Department with a chief complaint of a migraine.

Target Users: ED/UCC physicians, General Pediatricians, Pediatric Nurse Practitioners, Hospitalists

Guideline Inclusion Criteria:

- Children up to 18 years of age
- Physical exam normal
- History consistent with primary headache

Guideline Exclusion Criteria:

- Abnormal physical exam normal
- History inconsistent with primary headache

Clinical Questions Answered by Guideline:

1. Does a head CT scan compared to no head CT scan change the management of a child with migraine?
2. In the pediatric patient diagnosed with a refractory migraine, is Prochlorperazine an effective treatment compared to ketorolac, metoclopramide, sodium valproate, IV magnesium, droperidol, or promethazine?
3. 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 DHE?

4. In the pediatric patient diagnosed with a refractory migraine, does DHE vs. meperidine (IM); or DHE nasal spray; or IV valporate acid vs. IM DHE and metoclopramide decrease migraine pain or cure the migraine?
5. In patients with migraine, does treatment with intravenous magnesium sulfate alleviate headache?

Differential Diagnosis:

- Tension headache
- Cluster headache

Practice Recommendations:

Physical Exam:

The appropriate treatment for children and adolescents with migraine requires an individually tailored strategy; therefore, a thorough medical and family history and a complete physical exam is important. The physical exam needs to include:

- A blood pressure with the vital signs
- A complete neurologic exam that includes optic fundi examination (Lewis et al., 2004).

Diagnostics:

Neuroimaging. Neuroimaging (including computed tomography) in pediatric migraine headache has been demonstrated to **NOT** be effective (Graff, Kayyali, Alexander, Simon, & Morriss, 2008; Lateef, Grewal, McClintock, Chamberlain, Kaulas, & Nelson, 2009; Lewis, et al., 2002; Lewis, & Dorbad, 2000; Maytal, Bienkowski, Patel, Eviat, 1998; Romero, Picazo, Tapia, Romero, Diaz, & Romero, 1998) [**GRADE = Strong recommendation / Moderate-quality evidence**]. The American Academy of Neurology (AAN) makes the following recommendations on the neuroimaging of migraine headaches:

1. Obtaining a neuroimaging study on a routine basis is not indicated in children with recurrent headaches and a normal neurologic examination.
2. Neuroimaging **should be considered** in children with an abnormal neurologic examination (e.g. focal findings, signs of increased intracranial pressure, significant alteration of consciousness), the coexistence of seizures, or both.
3. Neuroimaging **should be considered** in children in whom there are historical features to suggest the recent onset of severe headache, change in the type of headache, or if there are features that suggest neurologic dysfunction (Lewis, Ashwal, Dahl, Dorbad, Hirtz, Prensky, & Jarjour, 2002).

Patient's pain assessment. Is the patient's pain assessment:

- > 3—Initiate **treatment**
- < 3—Discharge patient after providing the patient with the following discharge information*:
 - Migraine care card
 - Instruct to follow up with primary care provider

Treatment:

Prior to the initiation of pharmacologic interventions, all patients will have:

- Insertion of intravenous catheter for rehydration purposes: Normal Saline 20 mL/kg (maximum of 1 liter)
- Minimization of environmental stimuli:
 - Bright lights
 - Strong smells
 - Excessive loud noises
 - Cell phone/text message usage in room
 - Television usage
 - Keep patient door closed
 - Minimal visitation

All female patients ≥ 11 yoa must be tested via a urine pregnancy test; if pregnant the patient will not be able to progress further in this treatment guideline.

Initiation of treatment, first option.

Prochlorperazine (Compazine) is a well-studied phenothiazine medication which has shown clinical benefit in multiple pediatric research studies for the treatment of pediatric migraine (Brousseau, Duffy, Anderson, & Linakis, 2004) [**GRADE = Strong recommendation / Moderate-quality evidence**]. The recommended dosing of prochlorperazine is:

- 0.15 mg/kg, with a maximum of 10 mg (infused at 1 mg/minute) (Gunn & Nechyba, 2002).

Diphenhydramine (Benadryl) may be utilized with (or following) prochlorperazine therapy to prevent a dystonic reaction. Dosing of diphenhydramine is:

- 1 mg/kg, with a maximum of 50mg (slow IV push) (Gunn & Nechyba, 2002).

Discharge criteria[#]:

*After each medication intervention the patient should be assessed to determine if the patient meets the following **discharge criteria[#]**:*

1. Headache pain score ≤ 3 or decrease from initial pain score of $\geq 50\%$.
2. Normal neurological examination

If the patient meets the discharge criteria, discharge after providing the patient with the discharge information*.

Initiation of treatment, second option.

Valproic acid (VPA) may be an effective tool in the treatment of pediatric migraine (Edwards, Norton & Behnke, 2001; Reiter, Nickisch & Merritt, 2005) [**GRADE = Strong recommendation / Low-quality evidence**]. 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).

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If treatment failure occurs with first or second options other treatment options are:

Medication	Trade name	Category	Dose	Max dose	Formulations	Pt. charge	Contraindications	Adverse effects	Comments
<u>dihydroergotamine</u>	DHE	Misc	IM/SC: 0.5-1mg, repeat hourly if needed IV: 1mg, repeat hourly if needed	IM/SC: 3mg/day IV: 2mg/day Nasal: 4 sprays/day	IM/ SC /IV: 1mg/mL Nasal Spray: 4mg/mL or 0.5mg per spray	Inj: \$141 Nasal Spray: Not available at CMH&C	Other vasoconstrictive meds, severely impaired liver/kidney	Nasal: Rhinitis, dizziness, somnolence	Caution in adolescent females: Category X For further guidance regarding DHE use in pediatric migraine, please consult the <u>on-call pediatric neurologist</u> .
<u>sumatriptan</u>	Imitrex	Triptan	Nasal: 1 spray in one nostril, may repeat after 2 hours PO: 1mg/kg or 50-100 mg SC: 0.06mg/kg	Nasal: 40mg PO: 100mg SC: 6mg	Nasal Spray: 0.5mg/0.1mL SC: 12mg/mL	Nasal Spray: \$150 PO: \$105 SC: \$340	Ischemic heart disease, severe hepatic impairment, uncontrolled hypertension	Nasal spray: Bitter taste, flushing, dizziness, tingling sensation, mouth/tongue discomfort SC: Chest tightness, tingling sensation, injection site irritation	Nasal spray: Give flavored candy a few minutes before to mask bitter taste PO: Do not crush tablets
<u>promethazine</u>	Phenergan	Antiemetic	IV: 0.25-1mg/kg q4-6 hours PRN PO/PR: 0.25-1mg/kg q4-6 hours PRN	IV: 12.5mg PO / PR: 12.5mg	Inj: 2.5mg/mL PO: Syrup 6.25mg/5mL, Tablet: 12.5mg, 25mg Suppository: 12.5mg, 25mg	Inj / Suppository: \$25 PO: \$15 PR: \$25	Severe CNS depression, children <2	Tachycardia, bradycardia, hypotension, drowsiness, dry mouth, GI upset	Central line preferred or large vein access (not in wrist or hand)
<u>metoclopramide</u>	Reglan	Antiemetic	IV: 0.1mg/kg	IV: 10mg	Inj: 2.5mg/mL Tablets: 5mg, 10mg Liquid: 5mg/5mL	Inj: \$25 Tablets / Liquid: \$15	GI obstruction, pheochromocytoma, history of seizure disorder	EPS, hyper/hypotension, drowsiness, fatigue, tardive dyskinesia	Not for long term due to risks of tardive dyskinesia
<u>ondansetron</u>	Zofran	Antiemetic	IV: 0.15mg/kg PO: 0.15mg/kg (round to nearest 2mg)	IV: 8mg PO: 8mg	Inj: 2mg/mL PO: Solution 4mg/5mL, Tablet/ ODT: 4mg, 8mg	Inj: \$30 PO / Tablet / ODT: \$80		Tachycardia, bradycardia, headache, nervousness, rash, dry mouth	DOC if patient also suffering from nausea symptoms
<u>magnesium sulfate</u>	Magnesium sulfate	Misc.	IV: 50mg/kg over 20min	2 grams	Inj: 60mg/mL	Inj: \$25	Serious renal impairment, heart block, appendicitis	Flushing, hypotension, vasodilation, diarrhea	Watch for correct salt forms
<u>ketorolac</u>	Toradol	Analgesia	IV/IM: 0.5mg/kg PO: 0.25 mg/kg every 6 hours	IV: 30mg IM: 60mg PO: 40 mg/day	IV / IM: 15mg/mL Tablet: 10mg	Inj: \$30 Tablet: \$20	Active bleed, renal dysfunction, < 2 years old	Edema, drowsiness,	Tablet: Give with food or milk

Misc. = Miscellaneous; Inj = Injectable; ODT = Orally Disintegrating Tablets

Considerations when using other treatment options:

- DHE

Dihydroergotamine (DHE) is an ergot alkaloid which has been studied in the treatment of pediatric migraine headache. The safety and efficacy of DHE has been described in the pediatric and adult literature (Carleton et al, 1998; Edwards, Norton, Behnke, 2001; Fisher, Gosy, Heary, & Shaw, 2007). DHE is most effective for the refractory migraine headache which has failed other medications and interventions (Carleton et al, 1998; Edwards, Norton, Behnke, 2001; Fisher, Gosy, Heary, & Shaw, 2007) [**GRADE = Strong recommendation / Low-quality evidence**].

All patients must be pre-treated with metoclopramide (Reglan) at a dose 0.15 mg/kg (maximum 10 mg) 10 minutes prior to DHE infusion. DHE is dosed as an intravenous infusion at an initial dose of 0.25 mg IV over 5-10 minutes (in children > 40 kg). If this dose is tolerated, a second dose of 0.5 mg should be infused over 5-10 minutes. **For further guidance regarding DHE use in pediatric migraine, please consult the on-call pediatric neurologist.**

Common side effects of DHE infusion include burning at the site of infusion, leg cramps, nausea, and vomiting. All female patients receiving DHE require an evaluation for pregnancy (beta-HCG). Limitations to DHE use include the following: uncontrolled hypertension, chest pain, basilar migraine, or use of monoamine-oxidase inhibitors (MAOI's). DHE **should not be** used concomitantly (or within 24 hours) with "triptans" or cytochrome P-450 inhibiting (CYP450-3A4) medications (Gunn & Nechyba, 2002).

- Triptans

The 5-HT receptor agonists ("triptans") have been extensively studied in the treatment of pediatric migraine headache (Ahonen, Hämäläinen, Rantala, Hopp, 2004; Hämäläinen, Hoppu & Santavuori, 1997; Lewis, Hershey & Wasiewski, 2007; Rothner, Wasiewski, Winner, Lewis & Stankowski, 2006; Winner, Adelman, Aurora, Lener & Ames, 2006; Winner, Lewis, Visser, Jiang, Ahrens & Evans, 2002; Winner, Rothner, Wooten, Webster & Ames, 2006) [**GRADE = Weak recommendation / Moderate-quality evidence**]. Safety in the pediatric population has been well defined (Ahonen, Hämäläinen, Rantala, Hopp, 2004; Hämäläinen, Hoppu & Santavuori, 1997; Lewis, Hershey & Wasiewski, 2007; Rothner, Wasiewski, Winner, Lewis & Stankowski, 2006; Winner, Adelman, Aurora, Lener & Ames, 2006; Winner, Lewis, Visser, Jiang, Ahrens & Evans, 2002; Winner, Rothner, Wooten, Webster & Ames, 2006). Currently, the only "triptan" available at Children's Mercy Hospital is sumatriptan (Imitrex). The recommended dose and route of administration for the acute care setting is 0.06 mg/kg (maximum 6 mg) subcutaneously (SQ). Dosing of sumatriptan may be repeated for a total of two (2) doses in 24 hours – two hours must elapse between repeat doses of "triptans," including sumatriptan (Gunn & Nechyba, 2002).

There should be no more than two "triptan" doses in a 24 hour period, and two different "triptans" **should not be** utilized in the same patient. Limitations to triptan use include the following: uncontrolled hypertension, chest pain, basilar migraine, or use of monoamine-oxidase inhibitors (MAOI's). "Triptans"

should not be used concomitantly (or within 24 hours) with dihydroergotamine (DHE) (Gunn & Nechyba, 2002).

- Magnesium Sulfate

There is no evidence that intravenous magnesium sulfate improves pediatric migraine headache [*GRADE = Strong recommendation / Low-quality evidence*]. However, one small, adult study demonstrated migraine headache improvement in those patients with acute migraine with aura (Bigal, Bourdini, Tepper, & Speciali, 2002).

Does the patient meet discharge criteria[#]?

- If the patient does not meet discharge criteria, the patient should be admitted.
- If the patient meets the discharge criteria, discharge after providing the patient with the discharge information .

Outcome Measures:

The primary outcome measures for this guideline will be the rate of hospitalization and the total cost of medical evaluation for migraine headache patients pre- and post-implementation of the CPG. Other variables that will be evaluated in this study will include:

- a. Medication(s) administered
- b. Duration of stay in Emergency Department/Urgent Care Center
- c. Laboratory test(s) performed
- d. Neuroimaging performed
- e. Documentation of pediatric pain scores and improvement in aforementioned scores (if any)
- f. Percentage of times that the appropriate order set is used in patients with migraine headache
- g. Percentage of times that a medication outside the CPG is prescribed
- h. Percentage of patients who were re-evaluated at CMH following their initial outpatient evaluation using the Pediatric Health Information Systems database

Potential Cost Implications:

We propose that total costs will be decreased following implementation of the guidelines due to more efficient, stream-lined care with fewer hospitalizations and repeat ED visits.

Potential Organizational Barriers:

None known.

How guideline was piloted:

1. Discussed at Emergency Department Section meetings
2. Presented at Grand Rounds, 7/22/2010
3. Shared in E-Daily News

Guideline Preparation: This guideline was prepared by The Office of Evidence Based Practice (EBP) in collaboration with content experts at Children's Mercy Hospitals and Clinics. Development of this guideline supports the Department of Clinical Effectiveness's initiative to promote care standardization that builds a culture of quality and safety that is evidenced by measured outcomes. If a conflict of interest is identified the conflict will be disclosed next to the team members name.

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Guideline development funded by:

No external funding was obtained in the development of this guideline.

Development Process:

The review summary documents the following steps:

1. Review of existing internal and external guidelines and standards
 - a. Internal guidelines: No internal guidelines were identified
 - b. External guidelines: American Academy of Neurology Practice Parameter: Pharmacological treatment of migraine headache in children and adolescents was used to develop this guideline
2. Review preparation
 - a. PICOT questions established
 - b. Team leaders confirmed search terms used
3. Databases searched
 - a. AHRQ National Guideline Clearinghouse
 - b. Medline
 - c. Cochrane
 - d. CINAHL
4. Critically analyze the evidence
 - a. Guidelines
 - i. AGREE criteria were used to analyze published clinical guidelines

- b. Literature
 - i. CASP tools were used to analyze the literature (e.g. study limitations, consistency of results, directness of evidence, precision and reporting bias)
 - ii. GRADE criteria evaluated the literature based on:
 1. The balance between desirable and undesirable effects
 2. Patient values and preferences
 3. Resource utilization

The table below defines how the quality of the evidence is rated and how the recommendation is established based on the type of evidence:

Quality	Type of Evidence
High	Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies.
Moderate	Evidence from RCTs with important limitations (inconsistent results, methodological flaws, indirect evidence, or imprecise results) or unusually strong evidence from unbiased observational studies.
Low	Evidence for at least 1 critical outcome from observational studies, from RCTs with serious flaws or indirect evidence.
Very Low	Evidence for at least 1 of the critical outcomes from unsystematic clinical observations or very indirect evidence.
Recommendation	Type of Evidence
Strong	Desirable effects clearly outweigh undesirable effects or vice versa
Weak	Desirable effects closely balanced with undesirable effects

- 5. Recommendations for the guideline were developed by a consensus process incorporating the three principles of EBP (current literature, content experts, and patient and family preference [when possible]).

Approval Process: This guideline was reviewed and approved by the Content Expert Team, the Office of EBP, and other appropriate hospital committees as deemed suitable for the guidelines intended use. Dr. Jack Gladstein from the University of Maryland, Baltimore was the external reviewer of this guideline. Guidelines are reviewed and updated as necessary every 3 years within the Office of EBP at CMH&C. Content expert teams will be involved with every review and update.

Disclaimer:

The content experts and the Office of EBP are aware of the controversies surrounding Migraine. When evidence is lacking or inconclusive, options in care are provided in the guideline and the power plans that accompany the guideline.

These guidelines do not establish a standard of care to be followed in every case. It is recognized that each case is different and those individuals involved in providing health

care are expected to use their judgment in determining what is in the best interests of the patient based on the circumstances existing at the time.

It is impossible to anticipate all possible situations that may exist and to prepare guidelines for each. Accordingly these guidelines should guide care with the understanding that departures from them may be required at times.

Final

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