

Drug Therapy for Migraine Headache

Treatment Strategies

- Initially consider step-care starting with an appropriate trial of simple analgesics (e.g., aspirin, acetaminophen, OTC nonsteroidal anti-inflammatory drugs (NSAIDs), Excedrin¹).
- If unsuccessful, use stronger analgesics such as prescription-strength NSAIDs or combination products, such as Midrin.
- In patients with severe, incapacitating headaches with vomiting and prostration that are refractory to simple or combination analgesics, consider starting with the selective serotonin receptor agonists (SSRAs) or stronger analgesics², such as analgesic-sedative combinations (e.g., butalbital) with or without codeine, or prescription NSAIDs plus metoclopramide.
 - Limit opioids to patients with severe, but infrequent headaches, or the occasional headache that is unresponsive to either DHE or SSRAs. In patients with nocturnal headaches, the impact of side effects are not as problematic.
 - Opioids also may be an alternative in patients with menstrual migraine that does not respond to standard abortive agents.
 - Consider metoclopramide when specific migraine therapy does not relieve nausea and vomiting. As a gastric stimulant, it can help counter delayed gastric emptying caused by migraines.

Selective Serotonin Receptor Agonists (SSRAs)

- Imitrex injection provides the fastest onset of action (82% efficacy at 20 minutes) and may be most appropriate for severe migraines.
- Onset of pain relief with Imitrex nasal can occur as early as 15 minutes, but efficacy at two hours is less than the injection at 20 minutes (62% vs. 82%).³ Efficacy at two hours is comparable to that at four hours for oral preparations.
- Maxalt and Zomig may have an earlier onset of action than oral Imitrex or Amerge.^{4,5}
- Headache recurrence at 24 hours appears comparable for all SSRAs. The longer half-life of Amerge may contribute to a longer duration between recurrences.
- Though Maxalt-MLT does not work faster, patients with nausea may prefer that it dissolves on the tongue without the need to take with water.

¹ Lipton RB, Stewart WF, Ryan RE, et al. Efficacy and safety of acetaminophen, aspirin and caffeine in alleviating migraine headache pain. *Arch Neurol.* 1998;55:210-217.

² Ziegler DK. Opioids in headache treatment. Is there a role? *Neurol Clin.* 1997;15:199-207.

³ Moskowitz MA, Cutrer FM. Attacking migraine headache from beginning to end. *Neurology.* 1997;49:1193-1195.

⁴ Gaist D, Hallas J, Sindrup SH, Gram LF. Is overuse of sumatriptan a problem: A population based study. *Eur J Clin Pharmacol.* 1996;50:161-165.

⁵ Catarci T, Fiacco F, Argentino C, et al. Ergotamine-induced headache can be sustained by sumatriptan daily intake. *Cephalgia.* 1994;14:374-375.

- If unable to obtain relief with one SSRA, consider an alternative SSRA before resorting to opioid therapy.

Why Not Migranal?

- Intranasal DHE (Migranal) may provide a longer duration of action with lower recurrence rates than SSRAs, but its speed of onset is slower.
- Due to their vasoconstrictive effects, Migranal should not be used within 24 hours of serotonin agonists. Migranal should also not be used in pregnant women.

Costs

The Average Wholesale Price for acute therapy with the SSRAs or Migranal ranges from ~\$14 (Zomig 2.5 mg tablet) to ~\$19 (Imitrex nasal). Actual prices vary depending on discounts and rebates.

Daily Prophylactic (chronic) Therapy⁶

- Consider for patients with:
 - >2 headaches per month causing disability lasting 3 or more days, or
 - Infrequent, but severely incapacitating headaches, particularly when poorly controlled with abortive therapy, or
 - Abortive medication is required more than twice a week, or
 - Hemiplegic migraine or infrequent headaches that are profoundly incapacitating or that risk permanent neurologic injury.
- Prophylactic therapy may often be successfully tapered and discontinued in patients with well-controlled headaches.
- Consider prophylactic therapy a success if it reduces attacks by 50%. It may take 4 weeks before the initial effect and continues to increase for three months.

Efficacy of Prophylactic Drugs

Treatment Type	Efficacy		
	High	Low	Unproven
First-line	Beta-Blockers Tricyclic antidepressants Divalproex	Verapamil NSAIDs SSRIs ±	
Second-line	Methysergide ²³ Flunarizine MAOIs ^{8,24}		Cyproheptadine Gabapentin Lamotrigine

There is no evidence that prophylaxis using more than one drug is superior to monotherapy.⁷

⁶ Silberstein SD. Migraine: Diagnosis and Treatment. In: Silberstein SD, Lipton RB, Goadsby PJ, eds. Headache in Clinical Practice. Oxford, UK: Isis Medical Media; 1998.

⁷ Tfelt-Hansen P. Prophylactic pharmacotherapy of migraine. *Neurol Clin.* 1997;15:153-165.

± SSRIs = Selective serotonin reuptake inhibitors

‡ Significant adverse effects

§ MAOIs = Monoamine oxidase inhibitors

Beta-adrenergic Blocking Agents

- Propranolol produces an approximate 44% reduction in the frequency of attacks.⁸
- The cardioselective agents (e.g., atenolol, metoprolol) may be used in patients with asthma and other respiratory disorders.

Tricyclic Antidepressants

- Amitriptyline, in particular, has been shown to decrease the frequency, severity and duration of migraine attacks. Patients suffering from both insomnia and migraine might benefit the sedative effects.

Anticonvulsants

- Divalproex may be particularly appropriate for patients with co-existing epilepsy or mania.⁹
- Fatal hepatotoxicity is a serious side effect, but is rare in adults on monotherapy.

Calcium Channel Blockers

- Verapamil appears to be the most effective calcium channel blocker.
- Typically have a slow onset of action, ranging from 2-8 weeks.
- Consider for patients with comorbid hypertension or a contraindication to beta-blockers.
- Patients often report an initial increase in headaches that may effect compliance.

Development of Chronic Daily Headaches

Consider analgesic rebound headache if the patient reports:

- Analgesic (including OTC), SSRA or ergotamine use more than three times a week, and especially if daily use is reported.^{10,11}
- Headache duration exceeding 10 hours.
- The headaches are refractory; daily or nearly daily (>20 headache days/month) particularly with a low pain threshold.
- Headaches accompanied by asthenia, and nausea, and other gastrointestinal symptoms.
- Frequent early morning headaches.
- Increase in severity and frequency of headache attacks.

Medication withdrawal tends to result in spontaneous improvement. Prophylactic therapy does not seem effective.

⁸ Holroyd KA, Penzien DB, Cordingley GE. Propranolol in the management of recurrent migraine: A meta-analytic review. *Headache*. 1991;31:333-340.

⁹ Silberstein SD, Wilmore LJ. Divalproex sodium: Migraine treatment and monitoring. *Headache*. 1996;36:239-242.

¹⁰ Silberstein SD, Saper JR. Migraine: Diagnosis and Treatment. *In: Dalessio DJ, Silberstein SD, eds. Wolff's Headache and Other Head Pain*. New York, NY: Oxford University Press; 1993.

¹¹ Mathew NT. Transformed migraine, analgesic rebound, and other chronic daily headaches. *Neurol Clin*. 1997;15:167-185.

Consider drug misuse for patients with the following characteristics:

- A new patient with in-depth knowledge of a particular medication and its strengths and weaknesses.
- Evasive when asked about headache history, last episode, severity and frequency of attacks.
- Has specific medication requests and may be evasive about why regular physician was not contacted for advice or prescription renewal.
- Distinguish from transformed migraine where the patient typically describes an initial onset of migraines in their teens or 20s, eventually becoming more frequent. Eventually, the patient develops intercurrent paroxysmal tension-type headaches that merge with the migraines into chronic daily headache.

Suggested Internet Site

Much of the above information came from “Managing Migraine Today (II): Pharmacologic and Nonpharmacologic Treatment” on the JAMA Migraine Information Center Internet site (<http://www.ama-assn.org/special/migraine/migraine.htm>). We encourage you to visit this site for more information.