



Key Inforbits

- Introduction to migraines
- Diagnosis of migraines
- Non-pharmacological therapies
- Pharmacologic therapy
- New and upcoming treatments

June is... Migraine Awareness Month



INTRODUCTION TO MIGRAINES

- Statistics:
 - 17.1% of women report to have at least one migraine per year
 - 5.6% of men report to have at least one migraine
 - After the age of 12, females are three times more likely to suffer from migraines, possibly due to hormonal changes occurring during menstruation
 - Men and women between the ages of 30 and 49 have the highest prevalence.
 - Of the US population that have migraines:
 - 14% have \geq four attacks/month
 - 63% have one to four/month
 - 23% have <1 attack/month¹

DIAGNOSIS OF MIGRAINES

- Are you a migraneur?
 - Anyone can have a migraine, but recurrence is what sets migraineurs apart from other patients.¹
- A physical and neurological exam should be performed if a patient complains of a headache in order to exclude all other secondary causes of headaches, but diagnostic imaging should be avoided.
- Certain diagnostic criteria must be met in order to be diagnosed with migraines:
 - At least 5 attacks without aura and at least 2 attacks with aura
 - Headache attack lasting 4-72 hours
 - Headache has at least 2 of the following:
 - Unilateral location
 - Pulsating quality

- Moderate or severe pain
 - Aggravation or avoidance of routine physical activity
 - At least one present during headache:
 - Nausea
 - Photophobia
 - Not attributed to any other disease²
 - Aura is defined as fully reversible speech, sensory, and visual symptoms
 - At least one of the following must be present with aura:
 - One symptom that gradually develops over at least 5 minutes
 - Each symptom lasts for a minimum 5 min and max of 60 min
 - Headache that meets criteria without aura begins during the aura or within 60 min.
1. Minor DS, Wofford MR. Headache Disorders. DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey LM. Pharmacotherapy: A pathophysiologic approach. 9th ed. New York: McGraw-Hill Medical; c2014. Chapter 45; p. 2135-2167.
 2. Migraines. In: *DRUGDEX® System* [AUH SOP intranet database]. Version 5.1. Greenwood Village, CO: Truven Health Analytics. [updated Mar 19, 2015, cited 2015 Jun 2]. [about 50 p.]. Available from <http://www.micromedexsolutions.com/micromedex2/librarian/PFDefaultActionId/evidencexpert.DoIntegratedSearch#>

MIGRAINE NON-PHARMACOLOGIC THERAPY

Migraines are primarily treated with pharmacologic therapy; however there are some non-pharmacologic therapies to help alleviate or prevent headaches.¹

<p><u>Cold applications</u>- Cool wash cloths on the forehead or ice packs on the back of the neck can help distract from the pain of a migraine.</p>	<p><u>Isolation</u>- Isolation from external stimuli can also help. Avoiding light and loud noises by staying in a dark private room is an excellent example.</p>	<p><u>Prevention</u>- Identifying and avoiding triggers can help prevent migraines from ever developing. Common triggers include caffeine, alcohol, and sleep deprivation. A diary can help identify specific prompts.</p>
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ABORTIVE PHARMACOLOGIC MIGRAINE THERAPIES

Migraine therapies are broken into two categories, abortive and preventative.¹ Abortive therapies should be initiated at the onset of a migraine and include migraine-specific and non-specific medications. Migraine specific medications include ergots such as ergotamine or dihydroergotamine, and serotonin agonists such as sumatriptan or frovatriptan. Non-specific medications include general analgesics such as acetaminophen, ibuprofen, and aspirin.

So how do we know which abortive therapy to use? Simply put, we don't... exactly. Selection is based on two factors; both migraine severity and patient specific responsiveness to a medication.¹ Firstly, in general, migraine severity will determine if a migraine-specific or non-specific medication is more appropriate. For milder migraines, non-specific medications are usually more appropriate. For more severe migraines, more targeted therapies become appropriate.

Secondly, individual patient responsiveness will determine which medications are most suitable.¹ Discovering a patient's specific responsiveness to a medication takes time because no one medication works the same in every migraineur. It is a trial and error procedure. Some people respond better to ibuprofen and sumatriptan, where others may respond better to acetaminophen and ergotamine. Below are a list of abortive medication therapies with some advantages and disadvantages of each.

Some Guideline Recommended Treatments for Abortive Therapy

<p>Acetaminophen/aspirin/caffeine - This is a combination product, so it has multiple mechanisms of action. Acetaminophen use may be limited by alcoholism or concurrent acetaminophen therapies.^{1,2}</p>	<p>NSAIDs (Nonsteroidal Anti-inflammatory Drugs) - Comparable efficacy to serotonin agonists. May not be appropriate for anyone with renal disease or GI sensitivity to NSAIDs.^{1,3}</p>
<p>Serotonin Agonists- Migraine-specific. Sumatriptan comes in an injectable form, which has a faster onset than other dosage forms.^{1,4} Should not be used if there is a history of angina or heart attack. Cannot be used with ergots.</p>	<p>Ergots- Migraine-specific. Ergots have a black box warning that administration with certain medications could result in life-threatening peripheral ischemia.^{1,5} This includes protease inhibitors, macrolide antibiotics, and grapefruit juice. Cannot be used with serotonin agonists.</p>

PREVENTATIVE PHARMACOLOGIC MIGRAINE THERAPIES

Preventative medications are those that are either taken daily or just before a headache begins to help decrease the frequency and intensity of migraines.¹ People who need preventative therapy are those with symptoms that cause significant disability, have migraines that occur more than 2 times per week, and those who do not respond to or cannot take abortive therapies.⁶ These medications include butterbur, beta-blockers, anticonvulsants, antidepressants, NSAIDs, and serotonin agonists.^{6,7}

Preventative medications are selected based on patient specific factors and responsiveness to the medication. Patient specific factors are typically other disease states that may benefit from the same medications that are used to treat migraines. Also, some medications tend to work best in different people, so like abortive therapy there is a trial and error process. Listed are medications and things that may make them more or less appropriate for particular patients.

Some Guideline Recommended Treatments for Preventative Therapy

<p>NSAIDs and serotonin agonists- These are typically taken before migraines begin and not on a daily basis.^{1,3,4} They are appropriate for migraines that are predictable such as migraines that are associated with stressful times or menstrual cycles. NSAIDs are good nonspecific therapies for migraines that are not expected to be severe. Serotonin agonists are good migraine specific medications that are appropriate when more severe headaches are expected. Examples are:</p> <ul style="list-style-type: none"> • NSAIDs- fenoprofen, ibuprofen, ketoprofen, naproxen. • Serotonin agonists- frovatriptan, naratriptan, zolmitriptan.
<p>Beta-blockers- Taken daily.^{1,6,8} Best for patients who also have high blood pressure, anxiety, or angina.</p> <ul style="list-style-type: none"> • Beta-blockers- metoprolol, propranolol, timolol, atenolol, nadolol
<p>Butterbur- This is a natural, plant-based medication. The plant needs to be treated beforehand in order to make it safe; if consumed raw, the plant is carcinogenic.^{1,7} Taken once a day.</p>
<p>Anticonvulsants- These are also taken daily; most appropriate for migraineurs who also have seizures or manic-depressive disorder.^{1,6}</p> <ul style="list-style-type: none"> • Anticonvulsants- divalproex sodium, sodium valproate, topiramate
<p>Antidepressants- Taken daily would be best for someone also suffering from depression or insomnia.^{1,6} Examples are:</p> <ul style="list-style-type: none"> • Antidepressants- amitriptyline, venlafaxine

1. Minor DS, Wofford MR. Headache Disorders. In: DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey LM, editors. Pharmacotherapy: A pathophysiologic approach. 9th ed. New York: McGraw-Hill Education;c2014.Ch. 45
2. Acetaminophen. In: DRUGDEX® System (electronic version) [AUHSOP intranet database]. Greenwood Village, CO: Truven Health Analytics Inc.[updated 2015 June 1, cited 2015 June 3]. Available from: http://www.micromedexsolutions.com/micromedex2/librarian/ND_T/evidencexpert/ND_PR/evidencexpert/CS/8E7550/ND_AppProduct/evidencex

- [pert/DUPLICATIONSHIELDSYNC/15D53B/ND_PG/evidencexpert/ND_B/evidencexpert/ND_P/evidencexpert/PFActionId/evidencexpert.GoToDashboard?docId=004040&contentSetId=100&title=Acetaminophen&servicesTitle=Acetaminophen&brandName=Excedrin+Migraine#](#)
- Nonsteroidal Anti-Inflammatory Agents. In: Drug Facts and Comparisons (Facts and Comparisons eAnswers) [AUHSOP Intranet]. St. Louis: Wolters Kluwer Health/Facts and Comparisons [updated 2015, cited 2015 June 3]. Available from: <http://online.factsandcomparisons.com/MonoDisp.aspx?monoID=fandc-hcp11516&quick=12%7c31&search=12%7c31&isstemmed=True&NDCmapping=-1&fromTop=true#firstMatch>
 - Serotonin 5-HT₁ Receptor Agonists (Triptans). In: Drug Facts and Comparisons (Facts and Comparisons eAnswers) [AUHSOP Intranet]. St. Louis: Wolters Kluwer Health/Facts and Comparisons [updated 2015, cited 2015 June 3]. Available from: <http://online.factsandcomparisons.com/MonoDisp.aspx?monoID=fandc-hcp10008&quick=-14%7c31&search=-14%7c31&isstemmed=True&NDCmapping=-1&fromTop=true#firstMatch>
 - Ergotamine Derivatives. In: Drug Facts and Comparisons (Facts and Comparisons eAnswers) [AUHSOP Intranet]. St. Louis: Wolters Kluwer Health/Facts and Comparisons [updated 2015, cited 2015 June 3]. Available from: <http://online.factsandcomparisons.com/MonoDisp.aspx?monoID=fandc-hcp10773&quick=349468%7c3&search=349468%7c3&isstemmed=True&NDCmapping=-1&fromTop=true#firstMatch>
 - Silberstein S, Holland S, et al. Evidence-based guideline update: Pharmacologic treatment for episodic migraine prevention in adults. American Academy of neurology [Internet]. 2012 April 24 [cited 2015 June 3]. Available from: <http://www.neurology.org/content/78/17/1337.full.pdf+html>
 - Holland S, Silberstein S, Freitag F, et al. Evidence-based guideline update: NSAIDs and other complementary treatments for episodic migraine prevention in adults. American Academy of Neurology [Internet]. 2012 April 23 [cited 2015 June 3]. Available from: <http://www.neurology.org/content/78/17/1346.full.pdf+html>
 - Beta-Adrenergic Blocking Agents (Beta-Blockers). In: Drug Facts and Comparisons (Facts and Comparisons eAnswers) [AUHSOP Intranet]. St. Louis: Wolters Kluwer Health/Facts and Comparisons [updated 2015, cited 2015 June 3]. Available from: <http://online.factsandcomparisons.com/MonoDisp.aspx?monoID=fandc-hcp10293&quick=985723%7c3&search=985723%7c3&isstemmed=True&NDCmapping=-1&fromTop=true#firstMatch>

RECENT DEVELOPMENTS

First medical device to prevent migraine headaches... The U.S. Food and Drug Administration (FDA) allowed the marketing of the first medical device to prevent migraine headaches, Cefaly[®], in March 2014.¹ The device is a small, portable battery-powered device that is worn across the forehead and on top of the ears and is secured by a self-adhesive electrode. The device stimulates branches of the trigeminal nerve with electric current applied to the skin and underlying tissues. The patient may experience a tingling or massaging sensation when wearing the device. Cefaly[®] is indicated in patients 18 years or older to be applied 20 minutes once per day.



In the most recent trial assessing Cefaly[®] efficacy and safety, 2,313 patients with migraines were monitored for satisfaction with the device.² Almost one-half (46.6%) were not satisfied; however, the compliance check showed that the patients only used Cefaly[®] for 48.6% of the recommended time. The other 54.4% of patients were satisfied and were willing to purchase the device. Only 4.3% of patients reported side effects with Cefaly[®]; the most frequent were local pain, sleepiness/fatigue, insomnia, and headache after stimulation.

In an additional study, 67 patients were divided into a Cefaly[®] group and a placebo stimulation group.³ The average number of migraine days and use of medication for migraine pain decreased significantly in the Cefaly[®] group. There were no side effects reported in either group.

- Rodriguez J. FDA allows marketing of first medical device to prevent migraine headaches. FDA news release [Internet]. 2014 Mar 11 [cited 2015 Jun 3]. Available from: <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm388765.htm>.
- Magis D, Sava S, Sasso d'Elia T, Baschi R, Schoenen J. Safety and patients' satisfaction of transcutaneous Supraorbital NeuroStimulation (tSNS) with the Cefaly[®] device in headache treatment: a survey of 2,313 headache sufferers in the general population. J Headache Pain. 2013;14(95)1-8.
- Schoenen J, Vandersmissen B, Jeangette S, Horroelen L, Vandenheede M, Gerard P, Magis D. Migraine prevention with a supraorbital transcutaneous stimulator: a randomized controlled trial. Neurology. 2013;80(8)697-704.



The last "dose" ...

"Migraines got you TRIPpin'?" –Jeff Williams

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