

# Migraine Treatment from A to Z

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## **Definition and Characteristics of Migraine**

Migraine with aura and migraine without aura have replaced the older terms, “classical migraine” and “non-classical migraine.” In treating migraine, I usually do not differentiate between migraine with and without aura because the therapy generally remains the same.

Migraine without aura is a chronic idiopathic headache disorder with attacks lasting 4 to 72 hours. Status migrainosus applies to migraine headaches that exceed 72 hours. Migraine features often include a unilateral location, moderate or severe intensity of pain, and a throbbing or pulsating nature to the pain. There may be associated nausea, photophobia or phonophobia. Further characteristics include a positive relationship with menses, decreased frequency during pregnancy, increase of the pain with physical activity, and migraine in first-degree relatives. Seventy to 75% of migraine patients report a first-degree relative having had migraine.

A recurring headache that is moderate or severe and is triggered by migraine precipitating factors is usually considered to be migraine. These factors include stress, certain foods, weather changes, smoke, hunger, fatigue, etc. Migraineurs often have colder hands and feet than controls, and the prevalence of motion sickness is much higher in migraine patients. Most patients do not have all of the above characteristics, and there are certain diagnostic criteria that have been established by the International Headache Society for the definite diagnosis of migraine.

Distinguishing a milder migraine without aura from a moderate or severe tension headache may be very difficult, and I am not surprised when “pure” migraine medications are effective for severe tension headaches.

### **Table 1. Characteristics of a Migraine**

- Attacks are 4 to 72 hours
- Moderate or moderate-to- severe pain
- Patient history gives the diagnosis (not lab tests)
- Often occur in early morning (but may be anytime)
- Unilateral in one-half of patients
- One to five migraines per month is typical
- Gradual onset of pain is followed by a peak for hours, then slow decline
- Pain is throbbing, pounding, pulsatile or deeply aching
- Sharp “ice pick” jabs are common
- Peak ages are between 20 and 35 years
- 18% of women and 7% of men will experience a migraine in their lifetime; female ratio is 3:1
- Family history is often positive for migraine

Associated nausea, photophobia, blurred vision, phonophobia or dizziness are common, however, these may be absent

In women, there is often a positive relationship with menses

Cold hands and feet and motion sickness are common

I generally regard recurrent, repeated attacks of throbbing or severely aching headache as migraine, whether or not the patient has nausea, photophobia or phonophobia. This assumes that organic disorders, particularly brain tumors, have been ruled out.

The patient's history gives us the diagnosis of migraine. Physical exam and MRI or CAT scans are helpful only in ruling out organic pathology. Headaches that are of recent onset need to be investigated with an MRI scan. A check of intraocular pressure may be warranted. Although the pain is unilateral in 50% of migraineurs, the entire head often becomes involved. The pain may be in the facial or the cervical areas, and often will shift sides from one occurrence to another. Most patients, however, suffer the severe pain on one favored side from attack to attack.

The typical migraine patient suffers one to five attacks in a month, but many patients average less than one or more than 10 per month. The attack frequency varies with the seasons, and many patients can identify a time of year when their headaches increase significantly.

The pain of the migraine often follows a bell-shaped curve, with a gradual ascent, a peak for a number of hours, and then a slow decline. Occasionally, the pain may be at its peak within minutes of onset. Migraine pain is often throbbing, pounding or pulsatile, particularly when the patient's head is bent. The pain may simply be a steady, severe ache. Jabs of sharp pain, lasting seconds, are frequently experienced by migraineurs.

Most patients with migraine suffer some degree of nausea during the attack, and many patients have vomiting as well. The nausea is often mild, and some patients are not bothered by it. Many state that the headache is lessened after they vomit. Diarrhea occurs in some patients, and is usually mild to moderate. The presence of diarrhea renders the use of rectal suppositories very difficult.

Lightheadedness often accompanies the migraine, and syncope may occur. Most patients become very sensitive to bright lights, sounds and odors. In between migraine attacks, many patients retain the photophobia, and it is common for migraine patients to wear sunglasses most of the time. Sensitivity to bright lights is a distinctive migraine characteristic.

Pallor of the face is common during a migraine; flushing may occur as well, but is seen less often. Patients do complain of feeling excessively hot or cold during an attack, and the skin temperature may increase or decrease on the side with pain. Migraineurs often have cold hands and/or feet at all times.

Migraineurs often experience tenderness of the scalp that may linger for hours or days after the migraine pain has ceased. This tenderness may actually occur during the prodrome of the migraine. Both vascular and muscular factors contribute to the scalp tenderness.

Mild elevations in temperature are more commonly seen with migraines than is generally appreciated. Autonomic disturbances are relatively common, such as pupillary miosis or dilation, rhinorrhea, eye tearing and nasal stuffiness. These are also symptoms of cluster headache, including the sharp pain about one eye or temple.

Alterations of mood are seen with many patients prior to, during and after migraine attacks. Patients are usually anxious, tired or depressed. They often feel “washed out,” after an attack, but a calm or euphoric state occasionally is seen as a postdrome to the migraine. Rarely, euphoria or exhilaration may precede a migraine.

Weight gain due to fluid retention may occur, and begins prior to the migraine. At some point during the migraine, patients often experience polyuria. The weight gain is usually less than six pounds, and is transient.

## **Table 2. Somatic Symptoms Accompanying Migraine**

*Listed in order of frequency*

- Sensitivity to light
- Blurred vision
- Nausea
- Sensitivity to noise
- Tenderness about the scalp
- Dizziness or lightheadedness
- Lethargy
- Vomiting
- Sensitivity to odors
- Retention of fluid, with weight gain
- Photopsia
- Vertigo
- Anxiety
- Paresthesias
- Diarrhea
- Fortification spectra
- Nasal stuffiness
- Mild aphasia
- Syncope or near syncope
- Severe confusion
- Seizures
- Fever
- Hemiparesis or hemiplegia
- Ataxia or dysarthria (brain stem dysfunction)

## **Visual Disturbances**

Blurred vision is very common during migraine attacks, and is usually only mild or moderate. Approximately 20% of patient experience visual neurologic disturbances preceding or during the migraine; these auras may be as disturbing to the patient as the migraine pain itself. Most migraineurs experience the same aura with each migraine, but occasionally one person may have several types of auras. “The light of a flashbulb going off,” is the description many migraineurs give to their aura. The visual hallucinations seen most often consist of spots, stars, lines (often wavy), color splashes, and waves resembling heat waves. The images may seem to shimmer, sparkle or flicker. The above visual occurrences are referred to as photopsia.

Fortification spectra are seen much less often than photopsia. They usually begin with a decrease in vision and visual hallucinations that are unformed. Within minutes, a paracentral scotoma becomes evident and this assumes a crescent shape, usually with zigzags. There is often associated shimmering, sparkling, or flickering at the edges of the scotoma.

Patients may experience a “graying out” of their vision, or a “white-out” may occur. Some patients suffer complete visual loss, usually for some minutes. Photopsia may be experienced at the same time as the gray out, white out, or visual loss.

The visual symptoms usually last 15 to 20 minutes, and most often will be followed by the migraine headache. The aura may last as little as 1 to 2 minutes. Visual symptoms without the headache are common and are often very distressing to the patient.

## **Miscellaneous Neurologic Symptoms Associated with Migraine**

Numbness or tingling (paresthesias) are commonly experienced as part of the migraine. These are most often experienced in one hand and forearm, but may be felt in the face, periorally, or in both arms and legs. Like the visual disturbances, they often last only minutes preceding the pain, but the numbness may go on for hours, and at times the paresthesias are severe. The sensory disturbances usually increase slowly over 15 to 25 minutes, differentiating them from the more rapid pace seen in epilepsy.

Paralysis of the limbs may occur, but this is rare. This is occasionally seen as a familial autosomal dominant trait, and the term familial hemiplegic migraine is applied to this form. With the weakness, aphasia or slurred speech may also occur, and sensory disturbances are seen ipsilateral to the weakness.

Vertigo is occasionally experienced during the attack of migraine, and may be disabling. Ataxia may occur, but is not common. Rarely, multiple symptoms of brain stem dysfunction occur, with the term basilar migraine being applied to this type of syndrome. The attack usually begins with visual disturbances (most often photopsia), followed by ataxia, vertigo, paresthesias, and other brain stem symptoms. After 15 to 30 minutes, these severe neurologic symptoms usually abate, and are followed by a headache. This type of migraine often stops over months or years, and the patient is simply left with migraine headaches without neurologic dysfunction.

## **Workup for Migraine**

When patients present with a long history of typical migraine attacks, and the headaches are essentially unchanged, scans of the head are usually not absolutely necessary. The issue of testing for migraine has presented legal problems, for migraine patients may develop a brain tumor unrelated to the headache, and the legal system in the United States is very poor at deciding whether the physician was at fault for not obtaining a test. The preferred head scan for migraine is a MRI. The current ability to noninvasively obtain an angiogram (MRA) with the MRI allows us to detect most intracranial aneurysms.

Situations that raise the concern about organic pathology include: 1) progressive headaches over days or weeks, increasing in intensity; 2) new onset headaches, particularly in patients who “never” get headaches, or new onset exertional headaches; 3) neurologic symptoms or signs, stiff neck, papilledema, and changes in level of consciousness; 4) a fever that is not explained; 5) radical increase or change in a preexisting headache pattern.

The tests that are generally useful for diagnosis of headache are the MRI (brain) scan, the CAT (brain) scan, lumbar puncture, intraocular pressure testing, radiography or CAT scan of the sinuses, and blood tests. MRA is very valuable in the diagnosis of aneurysms. Whether to do any testing at all depends on the physician’s clinical suspicion of organic pathology. Although some patients request a “test” of their heads, the vast majority of chronic migraineurs are more likely to state that, “if I had a brain tumor, I would have been dead years ago.” Sound clinical judgment, based on patient history and a physical exam, is crucial in deciding who needs which exam.

The problems that need to be excluded in a patient with a new onset of migraine include: sinus disease, meningitis, glaucoma, brain tumor, arteritis, subarachnoid hemorrhage, idiopathic intracranial hypertension, hydrocephalus, pheochromocytoma, stroke or TIA, internal carotid artery dissection, and systemic illness. Excluding most of these problems is usually easily accomplished by the history and physical exam.

## **Management of Migraine**

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### **Keys to Management**

Watch headache triggers

Practice good sleep habits

Lose excess weight

Exercise daily, and practice yoga or another relaxation technique

Treat a migraine early in the headache

Do not overuse pain medicine; try to limit “as needed” medications to three days a week

If appropriate, treat with preventive medications

## **Headache Triggers**

With migraine and chronic daily headache sufferers, we like to emphasize avoidance of triggers. The most common triggers are: stress, weather changes, perimenstruation, missing meals, bright lights or sunlight, undersleeping, food sensitivity, perfume, cigarette smoke, after stress is over, oversleeping, exercise, and sexual activity. In general, headache patients do better with regular schedules, eating three or more meals per day and going to bed and awaking at the same time every day. Some foods can be headache triggers, but foods tend to be overemphasized.

Managing stress with psychotherapy, exercise, yoga, etc., often will reduce the frequency of headaches. With stress, it is not so much extreme stress, but daily hassles that increase headaches. When patients are faced with overwhelming daily stress, particularly when they cannot sleep well at night, headaches can be much worse the next day.

Relaxation techniques such as biofeedback, deep breathing, and imaging can be helpful for daily headache patients, particularly where stress is a factor. Yoga or Pilates may improve many elements of headache with benefits of stress management and muscle relaxation. The ideal would be to take a class weekly, then do the stretches and breathing for 10 minutes a day. Patients may see some relief from associated neck or back pain. Physical therapy can also help with these. Massage may also lessen symptoms, particularly neck pain. Patients can learn relaxation techniques from books or tapes that are readily available in bookstores, so that learning does not necessarily require extended visits to a therapist. However, working with a biofeedback therapist can be very useful, if patients are willing.

Many migraine patients have accompanying neck pain. Physical therapy or chiropractic treatment may help. Acupuncture is occasionally helpful. Massage can be effective, but the relief is short-lived. TMD may exacerbate migraine; with TMD, a bite splint is often useful.

Psychotherapy is extremely useful for many headache patients with regard to stress management, coping, life issues, family of origin issues, etc. Even though we may recommend psychotherapy, it is crucial to legitimize the headaches as a physical condition; they are not a “psychological” problem, but rather a physical one that stress may exacerbate.

## **Caffeine Use**

Whether in coffee, caffeine pills, or combination analgesics, it is necessary to limit the total caffeine intake. The maximum amount of caffeine to take each day varies from person to person, depending upon their sleeping patterns, the presence of anxiety, and their sensitivity to possible rebound headaches.

While caffeine can help headaches, the overuse of caffeine may increase headaches because of rebound mechanisms. Some patients do not suffer rebound headaches despite the ingestion of as much as 500 mg. of caffeine per day. Others develop rebound headaches with as little as 30 mg. daily. In general, try to limit caffeine to 150 or 200 mg. a day at most.

### **Table 3. Caffeine Sources**

*Limit caffeine to 150 mg. per day, or, at most, 200 mg. per day*

Coffee, brewed, 8 oz. cup: 75-125 mg. Drip is the strongest form, percolated is weaker. Specialty coffee brewers such as Starbucks may be up to 50% stronger than home-brewed. A small latte has 70-90 mg.

Instant: 40-150 mg. per cup, usually closer to 40 mg. Decaf: About 5 mg. per cup, but may be higher

Tea, 8 ounces: 30-50 mg.

Soft drinks: approximately 40 mg. per cup; energy drinks may have more than 200 mg. per 8 oz.

Chocolate: 1-15 mg. per ounce

Cocoa: 20-50 mg. per 8 ounces

Caffeine tablets: (NoDoz, Vivarin, Tired) contain 100 mg. of caffeine

Caffeine is also present in many analgesic medications, such as Excedrin Migraine (65 mg.), Anacin (32 mg.) and Vanquish (33 mg.)

### **Foods to Avoid**

Most people are sensitive to only two or three types of food in the diet. If a particular food is going to cause a headache, it will usually occur within three hours of eating. Compared to other triggers such as stress, weather, hormonal changes, missing meals, bright lights, and undersleeping, food sensitivities are not that common, but some patients are sensitive to the following:

Monosodium glutamate (MSG) – also labeled autolyzed yeast extract, hydrolyzed vegetable protein, or natural flavoring. Possible sources of MSG include broths or soup stocks, seasonings, whey protein, soy extract, malt extract, caseinate, barley extract, textured soy protein, chicken, pork or beef flavoring, meat tenderizer, smoke flavor, spices, carrageenan, seasoned salt, TV dinners, instant gravies, and some potato chips and dry-roasted nuts.

Alcohol. All alcohol can trigger a headache; beer and red wine are the worst offenders. White wine is not as likely to trigger a headache.

Cheese. Ripened, aged cheeses (Colby, brick, cheddar, Roquefort, brie, gruyere, bleu, Boursault, mozzarella, parmesan, Romano) and processed cheese are the worst. Less likely to trigger a headache: cottage cheese, cream cheese, and American cheese.

Chocolate

Citrus fruits

Meat that has been cured or processed, such as bacon, bologna, ham, hot dogs, pepperoni, salami, sausage; canned, aged or marinated meats.

Nuts, peanut butter

Yogurt, sour cream

Large amounts of aspartame (NutraSweet)

## **Medications: Abortives**

Most people with migraines do not need preventive medicines, particularly patients without comorbidities, or only a few headaches. How many headaches a month are too many? There is no absolute rule that applies to headache treatment. For a patient with two headaches a month that are severe, prolonged and not relieved by drugs, we might use preventive medicine. For another person with five headaches a month, who can take an Excedrin or triptan and obtain relief, we may not choose preventive medicine, because all medicines have their possible side effects. The choice of medications depends on age, medical and psychiatric comorbidities, frequency and severity of the migraine, and patient input. The patient should play an active role in medication choice.

### **First Line Migraine Abortive Medications**

#### ***Triptans***

Over 200 million patients worldwide have used triptans. The most effective way to use triptans is to take them early in the headache. Sumatriptan is an extremely effective migraine abortive medication with minimal side effects. It is effective for approximately 70% of patients and has become the gold standard in abortive headache treatment. The earlier one uses any triptan the better the effect. The usual dose is one tab every three hours as needed, but not more than twice a day. We do need to limit triptan use, ideally to three days a week at most, so as to avoid rebound or medication-overuse headache (MOH).

The triptans are helpful for moderate as well as more severe migraines. Certain patients tolerate one of the triptans better than another and it is worthwhile to try several in an individual patient. Triptans are an excellent choice for migraine patients who are not at risk for coronary artery disease. Patients in their 50's or 60's can use these drugs, but they should be prescribed cautiously, and only in those patients who have been screened for CAD.

#### ***A Summary of the Triptans***

**Sumatriptan** (Imitrex): The usual oral dose is one 50 mg. or 100 mg. tablet, q 2-3 hours, 200 mg. per day at most. The SQ Imitrex (4 or 6 mg.) is the most effective migraine abortive for severe, faster onset migraines. It is also available as a nasal spray. Over 100 million people have used Imitrex, and it has been utilized for nearly 20 years. The addition of an NSAID to a triptan may enhance efficacy and prevent recurrence.

**Treximet** (sumatriptan plus naproxen) is an excellent combination drug that helps to prevent recurrence of the headache. The usual dose is one every three to four hours, two in a day at most. The addition of naproxen may cause stomach pain or nausea.

**Sumatriptan Injections** (Imitrex STATdose, Sumavel DosePro, Alsuma, or generic prefilled syringes). Sumatriptan injections are available in the Imitrex STATdose injector form and the needle-free Sumavel DosePro. Although the usual dose had been 6 mg., the 4 mg. STATdose is often effective. Sumavel DosePro is easier to use than STATdose. The injections are dosed at one every three to four hours as needed, but limited to two per day. Alsuma is a new "epi-pen" device with 6 mg. of sumatriptan. The vials of sumatriptan, 6 mg per 0.5 cc, are also available. The patient draws up 0.25 cc (3 mg. Imitrex) or



0.5 cc (6 mg.) into an insulin syringe. There are also generic, pre-filled syringes of 6 mg. sumatriptan which are easy to use.

**Rizatriptan** (Maxalt) is very similar to Imitrex. Maxalt is very effective for migraine. The usual dose is one standard 10 mg. tablet, or the 10 mg. Maxalt MLT (rapidly disintegrating tablets) which are placed on the tongue. These rapidly disintegrating tablets have a pleasant taste and may be taken without water. Side effects are similar to those of Imitrex. Maxalt is very well tolerated. It will be available as a generic in 2012.

**Eletriptan** (Relpax) is an effective and well-tolerated triptan. It is available in 20 and 40 mg. strengths; 40 mg. is the usual dose. The side effects, in general, have been found to be fairly minimal. They include possible nausea, pressure in the throat, dizziness and tiredness or weakness.

**Zolmitriptan** (Zomig), in 2.5 mg. or 5 mg. tablets, is another very effective abortive. The usual dose is 5 mg. every three to four hours, as needed, two per day at most. Zomig ZMT, 5 mg., is a pleasant-tasting, dissolvable tablet. Like Maxalt MLT, it provides an alternative to the oral tablets.

**Frovatriptan** (Frova) is well tolerated. The long (26 hours) half-life is advantageous for those with prolonged migraines. Mean maximal blood concentrations are seen approximately 2 to 4 hours after a dose of Frova. Frova has been particularly useful for those with slower-onset moderate or moderate to severe migraines. Frova is available in 2.5 mg tablets. Frova has been effective for preventing menstrual migraines.

**Almotriptan** (Axert) is very similar to the other triptans, and effective for migraine headache. The usual dose is one 12.5 mg. tablet, every 3 to 4 hours, limit of two per day. Side effects are similar to those of the other triptans. Axert combines good efficacy with excellent tolerability. In 2009, Axert gained an official FDA-indication for use in adolescents with migraine.

**Naratriptan** (Amerge) is a milder, longer-acting triptan. A generic form is now available. The usual dose is every three to four hours as needed, but limited to two per day at most.

### **Non-Triptan First Line Abortives for Migraine**

**Cambia** (diclofenac potassium). Cambia is an excellent new migraine abortive. It is useful in younger patients and in older ones who can tolerate NSAIDs. It is a 50 mg. diclofenac packet to be mixed with water; it is available in boxes of three or nine packets. The usual dose is one packet, which may be repeated every two to four hours, with a limit of three packets in a day at most. Typical side effects of NSAIDs, primarily GI, may occur. Cambia may be combined with triptans. Caffeine may be added to increase efficacy.

**Excedrin** (or Excedrin Migraine). Useful as an over-the-counter preparation, it contains 250 mg. aspirin, 65 mg. caffeine, and 250 mg. acetaminophen. Anxiety from the caffeine or nausea from the aspirin is common. One or two tablets every three hours is an effective dose for patients with mild or moderate migraines. Tension Excedrin is also available, but is less effective. It contains acetaminophen plus

caffeine. Rebound headache may occur with overuse; four per day (but not on a daily basis) should be the maximum.

**Naproxen** (Anaprox, Aleve). Useful in younger patients, naproxen is occasionally helpful for menstrual migraine. It is non-sedating, but patients frequently report GI upset. The usual dose is 500 mg. with food or a Tums to start; it may be repeated in one hour if no severe nausea is present, and again in three or four hours. Limit to three per day at most. Available over-the-counter as Aleve, 220 mg., or generic. Adding caffeine increases efficacy. Naproxen may be used at the same time as a triptan.

**Ibuprofen** (Advil, Motrin). Available over-the-counter, and approved for children. Liquid Advil is also available. Occasionally useful in treating menstrual migraine; GI side effects are common. The usual dose is 400 to 800 mg., every three hours, limiting the total dose to 2,400 mg. per day. Combining ibuprofen with caffeine may be helpful. The short half-life is a drawback. May be used with triptans, even at the same time.

**Prodrin** (similar to generic Midrin, which has an added sedative and does not contain caffeine) Prodrin capsules are a combination of 20 mg. caffeine, 65 mg. isometheptene, and 325 mg. acetaminophen. Isometheptene is a mild vasoconstrictor. The usual dose is one capsule every two to three hours as needed. Due to the caffeine, limit these to two or three a day, with some exceptions. Prodrin is non-sedating and non-addictive. The caffeine may cause nervousness or a faster heartbeat. Patients with insomnia should not use it after 3 P.M. or so. Patients with high blood pressure should use Prodrin with caution, and only if the blood pressure is controlled. Prodrin is helpful for migraines as well as less severe headaches. It fits the need for a non-addicting medication that does not cause drowsiness. The availability of Prodrin varies. If it is not available, generic Midrin, which has a sedative and no caffeine, is usually used, along with additional caffeine.

## **Second Line Abortive Medications for Migraine and CDH**

**Ketorolac** (Toradol; generic is available). The injections are much more effective than the tablets. Patients may use the injections at home, 60 mg. per 2 cc. The usual dose is 60 mg., which may be repeated in one hour if necessary. Nausea or GI pain may occur. Ketorolac is nonaddicting and does not usually cause sedation. Limit to three per week due to possible nephrotoxicity. IV Ketorolac is very effective. There is a new nasal spray form of Toradol, "Sprix." Sprix may produce a burning feeling in the throat.

**DHE.** (Migranal is the brand name of DHE Nasal Spray. Inhaled form (Levadex) is awaiting FDA approval). Effective as an IV or IM injection, and occasionally as a nasal spray. A new, inhaled form, Levadex, is pending FDA approval, and indications are that it may be an excellent abortive. All forms of DHE are safe and well tolerated. Nausea, leg cramps, and burning at the injection site are common. IV DHE is very effective in the office or emergency room. One mg., IM or IV, is the usual dose, but this may be titrated up or down. If it is the first time a patient has used DHE, start with  $1/3$  or  $1/2$  cc only.

**Butalbital.** (Fiorinal, Fioricet, Esgic, Phrenilin) Fiorinal contains ASA, butalbital, and caffeine; Fioricet, Phrenilin and Esgic replace the ASA with acetaminophen. Generics of these compounds may not work as well. These medications are addicting, but very effective for many patients. Dosage is one or two tablets

or capsules every three hours, with a limit of 30 or 40 pills per month at most. Fiorinal #3, or Fioricet with codeine, adds 30 mg. of codeine and is more effective than plain Fiorinal or Fioricet. Esgic Plus adds additional acetaminophen to Esgic. Phrenilin contains no aspirin or caffeine, and is very useful at night, or in those with GI upset. Short-lasting tiredness and spacey or euphoric feelings are common side effects. Butalbital must be used sparingly in younger people.

**Opioids.** (Fiorinal with codeine, Vicoprofen, Vicodin, oxycodone, meperidine, etc.) PO or IM, these are often the best of the 'last resort' approaches. When given IM, they are usually combined with an antiemetic. While addiction is a potential problem, the difference between dependency and addiction is crucial to understand. Ultram (tramadol is the generic) is milder, with relatively few side effects. Vicoprofen combines 7.5 mg. of hydrocodone with 200 mg. ibuprofen; generic is available. It is more effective than the other hydrocodone preparations because of the addition of ibuprofen, and generally is well tolerated. Actiq (Fentanyl oral) has been used in several small studies, but is not indicated for this use. Opioids should be used sparingly in younger patients.

**Corticosteroids.** Cortisone is often the most effective therapy for severe, prolonged migraine. Dexamethasone (Decadron) or Prednisone are the usual oral forms, and are dosed at 4 mg. of Decadron or 20 mg. of Prednisone, 1/2 or 1 every 8 to 12 hours, as needed. Smaller doses may also be effective. Three tablets a month is the usual maximum. These are very helpful for menstrual migraine. The small doses limit side effects, but nausea, anxiety, a "wired" feeling and insomnia are seen. IV or IM steroids are very effective as well. Patients need to be informed of, and accept, the possible adverse events.

**Ergots.** These older vasoconstrictors have many side effects, but are often effective. At most, use on only two days out of seven. Nausea and anxiety are common with ergotamine compounds. Cafergot adds caffeine to the ergotamine. Only compounded Cafergot PB is available. The suppositories are more effective than the tablets. Rebound headaches are common with overuse of ergots. Use with caution after age 40, particularly with cardiac risk factors. Ergomar SL tabs are back on the market. Ergomar is an excellent brand, pure ergot with no caffeine. The Ergomar dose is 1/2 or 1 tab once or twice a day PRN.

**Miscellaneous Approaches.** Muscle relaxants (Soma, Valium) or tranquilizers (Klonopin, Xanax) are occasionally useful, primarily to aid in sleeping. IV Depacon (sodium valproate) is safe and can be effective. The "atypical antipsychotics," such as Zyprexa or Seroquel, may be occasionally useful on an as-needed basis. In the ER, IV Compazine or Reglan may be useful. Certain preventive medications (Depakote, Topamax, amitriptyline) may be useful on an as-needed basis, utilizing low doses every 4 to 6 hours PRN. The antihistamine Benadryl is occasionally useful IM.

### **Antiemetic Medications**

*These are commonly prescribed for nausea and other GI symptoms.*

**Promethazine** (Phenergan): Mild but effective for most patients. Very sedating, but with a low incidence of serious side effects. Available as tablets, suppositories and oral lozenges (which are formulated by compounding pharmacists). Used for children and adults.

**Prochlorperazine** (Compazine): Very effective but there is a high incidence of extrapyramidal side effects. Anxiety, sedation and agitation are common. Given intravenously, it may stop the migraine pain as well as the nausea. Tablets, long-acting spansules, and suppositories are available.

**Metoclopramide** (Reglan): Mild, but well tolerated; commonly used prior to IV DHE. Fatigue or anxiety do occur, but usually are not severe. Five to 10 mg. are given PO, IM or IV. It is in Pregnancy Category B (relatively safe).

**Trimethobenzamide** (Tigan): Well tolerated, useful in children and adults. Tablets, suppositories or oral lozenges may be used; lozenges are formulated by compounding pharmacists.

**Ondansetron** (Zofran; generic is available) Dose is 4 or 8 mg. PO. A very effective antiemetic with few side effects, but very expensive. It is not sedating. Zofran is extremely useful for patients who need to keep functioning and not be sedated with an antiemetic. Available as oral tablets or as Zofran ODT (orally disintegrating tablets). It is in Pregnancy Category B (relatively safe).

## **Preventive Medications: Long-term Results**

The goal with preventives is to help reduce the headache's intensity by 25 to 75%. If patients think their headaches are going to be completely cured, they may come back and say, "The medicines are not working because I still have some migraines." They may be 50% better, which is often as good as we can achieve. Headache diaries can help, but we also need to convey realistic goals to the patient. In my experience, only half of patients do well on long-term preventives. I've done two long term studies, looking at usage over a year's time, with a total of nearly 800 patients on preventives. Only 46% found any preventive they could tolerate and that worked for at least nine months. The other group discontinued preventives for various reasons. We have a long way to go, and we need much better preventives.

### ***What Patients Need to Know Prior to Starting a Preventive***

In using medication, a realistic goal is to decrease the tension headache severity by 70%, not to completely eliminate the headaches. It is wonderful when the headaches are 90% improved, but the idea is to minimize medication. Most patients need to be willing to settle for moderate improvement.

Patients with more than three migraines per month that are not well-controlled may be candidates for preventives. Those with chronic daily headache are more likely to need preventives. A preventive is chosen with regard to the type of headache and comorbidities, such as anxiety, depression, GI upset, etc. Preventives may take 3 to 6 weeks to work, and there may be only a 50% improvement. The patient must accept this, and be willing to tolerate the possible side effects.

Patients must be willing to change medications when necessary. They need to be aware that what is effective for someone else may not work for them. Trial and error is often used to find the best preventive approach for a person. Preventive medications may take weeks to become effective. The doses often need to be adjusted, and thus patience is necessary with these medications. The physician

needs to be available for phone consultations pertaining to the headaches and medicine. In the long run, preventive medications are effective for approximately 50% of patients.

Preventive medications are individualized toward the patient's needs, and the patient's input is very important. We select a particular preventive depending upon the person's comorbidities, GI system, medication sensitivities, etc. Fatigue is another major reason for patients abandoning a preventive medication. Headache patients commonly complain of fatigue, and tend to give up on medications that increase tiredness. A patient's occupation also may guide us away from certain medications; for example, an accountant may not be able to tolerate the memory problems associated with topiramate.

Side effects are possible with any medication; a patient has to be prepared to endure mild side effects in order to achieve results. We cannot stop one medication and switch to another because of very mild side effects. Most patients are willing to put up with mildly annoying side effects. Most preventive medications are utilized in medicine for another purpose. Patients should be informed that Elavil, for instance, is also used for depression, although it is usually in much higher doses. Patients using Elavil should be told why, and be reassured that it is not because they are depressed.

### ***Natural Supplements and Herbs for Headache***

Feverfew, Petadolex (butterbur), and magnesium oxide have all proven effective in double-blind studies as migraine preventives. Of these, Petadolex has been the most effective. Omega-3 fatty acids may help headaches, and are an excellent supplement for general good health.

**Petadolex** is commonly used in Europe, and this herbal preparation has been successful in preventing migraines in several well-designed blind studies. The usual dose is 50 mg., twice a day. Earlier concerns about carcinogenesis with this family of herbs have decreased with Petadolex, which is a purified form of the herb butterbur. Patients have occasionally experienced GI upset or a bad taste in the mouth, but Petadolex is usually well tolerated. It is prudent to stop it every three months or so. Available by calling 1-888-301-1084 or through [www.petadolex.com](http://www.petadolex.com).

**Magnesium** is a naturally occurring mineral which helps many systems in the body to function, especially the muscles and nerves. It has been shown that magnesium levels in the brain of migraine patients tend to be lower than normal. Magnesium oxide is used as a supplement to maintain adequate magnesium in the body. A dose of 400 or 500 mg. per day can be used as a preventive; tablets are found in most pharmacies. However, mild GI side effects may limit use. There are also complications from drug interactions, and kidney and other diseases.

**Feverfew** has been demonstrated to be mildly effective in some patients for prevention of migraine headache. Feverfew can cause a mild increased tendency toward bleeding, and should be discontinued two weeks prior to any surgery. The problem with many herbal supplements is quality control. The amount of parthenolide (the active ingredient in feverfew) varies widely from farm to farm; certain farms consistently have better quality than others. Eclectic Institute uses a process that freeze-dries the herbs, making the product highly reliable. It is available in health food stores and at Whole Foods. The usual dose is 2 capsules each morning. Patients occasionally will be allergic to feverfew, and it should not be used during pregnancy.

## First Line Preventive Medications for Migraine

**Botulinum Toxin Injections.** Botulinum toxin A (Botox) has been studied extensively in migraineurs. Almost 3 million people have had Botox injections for headache. Approximately 50 to 60% of patients have significant relief after treatment. The Botox brand is the only one with FDA approval for treatment of chronic migraine. While it is expensive, Botox is relatively safe and only takes a few minutes to inject. One set of injections can decrease headaches for one to three months. Botox may be safer than many of the medications that are utilized for headache. There is also a cumulative benefit, where the headaches continue to improve over a year of injections.

**Topiramate (Topamax).** Topiramate is FDA approved as a migraine preventive. This anti-seizure medication is utilized for migraine, CDH, and cluster headache. It does not irritate the liver. Sedation and cognitive side effects, such as confusion or memory problems, may limit its use. Topiramate often decreases appetite, which leads to weight loss; this is unusual among headache preventives. The starting dose is 25 mg. once or twice daily; this may be pushed to 100 mg. once or twice per day. 100 mg. daily is the usual dose. It is usually well-tolerated in lower doses, and may be effective as a mood stabilizer for some milder bipolar patients. GI upset may occur. Acute glaucoma has been a rare side effect. The risk of forming kidney stones is increased by the use of topiramate. Bicarbonate levels should be monitored, as topiramate may cause a dose-related metabolic acidosis.

**Valproate (Depakote).** This seizure medication is a long time staple, popular for migraine prevention. It is usually well tolerated in the lower doses utilized for headaches. The generic may not be as effective. Liver functions need to be monitored in the beginning of treatment. Side effects include lethargy, GI upset, depression, memory difficulties, weight gain and alopecia. Dosage ranges from 250 to 1500 mg. per day, in divided doses. The average dose is 500 to 1000 mg. per day. Levels need to be checked for toxicity on the higher doses. Depakote is also one of the primary mood stabilizers for bipolar. Available in 125, 250 and 500 mg. tablets. Depakote ER (500 mg.) is an excellent long-acting tablet that may be dosed at once daily; Depakote 250 ER is also available. As with most preventives, Depakote needs four to six weeks to become effective. It is FDA-approved for migraine prevention. Depakote should not be used during pregnancy.

**Beta Blockers.** Effective for migraine, and occasionally effective as a preventive for daily headaches. Long-acting (LA) Inderal capsules may be dosed once per day. Sedation, diarrhea, lower GI upset and weight gain are common. Very useful in combination with amitriptyline. Dosage begins with the long-acting at 60 mg., and is usually kept between 60 and 160 mg. per day. Lower doses are sometimes effective, such as 20 mg. BID of propranolol. Other beta-blockers are also effective, such as metoprolol (Toprol XL) and atenolol. Some of these are easier to work with than propranolol because they are scored tablets, and metoprolol and atenolol have fewer respiratory effects. Depression may occur. Beta blockers are useful for those with concurrent hypertension, tachycardia, panic, anxiety, and MVP. Nebivolol (Bystolic), may be helpful for headaches, and has fewer respiratory side effects.

**Amitriptyline (Elavil and other tricyclics).** Effective, inexpensive and also useful for daily headaches and insomnia. Use in low doses, at night. Sedation, weight gain, dry mouth and constipation are common. Starting dose is 10 mg., working up to 25 or 50 mg.; can be pushed up to 150 mg., or decreased to 5 mg. Other tricyclic antidepressants such as doxepin and protriptyline can be effective for migraine.

Nortriptyline is similar to amitriptyline, with somewhat fewer side effects. These are also used for daily tension-type headaches. Protriptyline is one of the few older antidepressants that does not cause weight gain. However, anticholinergic side effects are increased with protriptyline. While the SSRI's are utilized, they are more effective for anxiety and depression than for migraine. Tricyclics are more effective for pain than are the SSRI's.

**Naproxen** (Naprosyn, Naprelan, Anaprox, Aleve, and other NSAIDs). Useful in younger patients, once a day dosing. It is particularly useful for menstrual migraine and sometimes helpful for daily headaches. Naproxen is nonsedating, but frequently causes GI upset. Effective as an abortive, it may be combined with other first line preventive medications. The usual dose is 500 or 550 mg. once a day, but this may be pushed to twice a day. Other anti-inflammatories can be utilized for prevention of migraine. As with all anti-inflammatories, GI side effects increase as people age, and so these are used much more in the younger population. With daily NSAIDs, blood tests are needed to monitor liver and kidney function.

**Verapamil.** Reasonably effective for migraine; once a day dosing with the slow release (ER) tablets. Usually nonsedating, and weight gain is uncommon. Occasionally helpful for daily headaches, it may be combined with other first line medications, particularly amitriptyline or naproxen. Constipation is common. Starting dose is 1/2 of a 240 mg. ER tablet, increasing quickly to one 240 mg. tablet per day. May be pushed to 240 mg. twice a day, or decreased to 120mg. or 180 mg. per day. With doses higher than 240 mg. daily, an EKG needs to be done.

**Natural Supplements and Herbs.** Many patients prefer to start with the natural preventives. Petadolex, a safer form of the herb butterbur, has been the most effective natural preventive. It has held up well in multiple trials. It is widely used in our office and has proven effective for all ages.

## **Second Line Migraine Preventive Therapy**

**Gabapentin** (generic available; Gralise is long-acting gabapentin, taken once or twice a day). Gabapentin is an anti-seizure medication that has been demonstrated to be useful in migraine and tension headache prophylaxis. Tablets are available in 100, 300, 400, 600 and 800 mg. sizes. The usual dose for headache prevention is 600 to 2400 mg. per day. In a large study on migraine, doses averaged around 2,300 mg. per day, but lower doses are usually prescribed. Some patients do well with very low doses (200 or 300 mg. per day). Sedation and dizziness may be a problem; however, gabapentin does not appear to cause end-organ damage, and weight gain is relatively minimal. Gabapentin can be used as an adjunct to other first line preventive medications. The generic, gabapentin, is now widely in use. A newer drug, Lyrica (pregabalin), has a similar mechanism of action to gabapentin. Lyrica is an anti-seizure drug, useful also for preventing pain. Side effects are similar to those of gabapentin. The dose of Lyrica varies from 25 mg. BID to 150 mg. TID.

**Polypharmacy.** Two first line medications are used together. The combination of two preventives is more effective than one drug alone. Depakote is often combined with an antidepressant. Amitriptyline may be combined with propranolol, particularly if the tachycardia of the amitriptyline needs to be offset by a beta-blocker; this combination is commonly used for "mixed" headaches (migraine plus chronic daily headache.)

The NSAIDs may be combined with most of the other first line preventive medications. Thus, naproxen is often given with amitriptyline, propranolol or verapamil. Naproxen is employed simultaneously as preventive and abortive medication. Polypharmacy is commonly employed when significant comorbidities (anxiety, depression, hypertension, etc.) are present.

**Tizanidine and Cyclobenzaprine.** A safe, non-addicting muscle relaxant, tizanidine is useful for migraine and CDH. The usual dose is one or two 4 mg. tablets qhs; the 4 mg. tablets are double-scored, so that patients may begin with 1/4 or 1/2 tablet. Sedation and dry mouth are common. Tizanidine may be used on a PRN basis for milder headaches, or for neck or back pain. A 2 mg. tablet is also available.

Cyclobenzaprine (10mg) is helpful for sleeping, and helps some with migraine and CDH. A half- tablet may be used. Sedation is a common side effect.

**Ace inhibitors and ARB's.** There have been a number of studies on this category of blood pressure meds; ARB's are preferred due to the minimal side effects. Examples include Cozaar (losartan), Benicar, and Atacand. For the patient with HTN and migraine, these may be useful. Side effects include dizziness, among others, but they are usually well tolerated, with no sedation/weight gain.

**SNRI Antidepressants** (Effexor XR, Cymbalta, Pristiq) Effexor XR is an excellent antidepressant; used primarily as a SSRI at lower doses, and at 100 to 150mg., norepinephrine is also increased. The generic form of Effexor may not be as effective. The antidepressants with dual mechanisms (serotonin and norepinephrine are more effective for pain and headache. Doses vary from 75 mg. to 225 mg., and Effexor XR is particularly useful for anxiety with depression. Pristiq is an excellent newer version of Effexor. Duloxetine (Cymbalta) also has a dual mechanism of action, and has been useful for pain; usual dose is 30 to 60 mg. daily. Pristiq is very similar to Effexor, and is available in 50 mg. and 100 mg. tablets.