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ROBBINS HEADACHE CLINIC

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INFORMATION FOR HEADACHE PATIENTS

Non-Medication Strategies for Headache Patients

With migraine and chronic daily headache sufferers, we like to emphasize avoidance of triggers. The most common triggers are, in descending order: stress, weather changes, perimenstrually, missing meals, bright lights or sunlight, undersleeping, foods, perfume, cigarette smoke, after stress is over, over sleeping, exercise, and sexual activity.

Headache patients, in general, do better with regular schedules, eating three or more meals per day and going to bed and awakening at the same time every day. Managing stress with psychotherapy, exercise, yoga, etc., often will reduce the headaches. The “headache foods” tend to be overemphasized as a headache trigger.

Exercise for 15 to 20 minutes per day (or more) is often helpful for headache patients; if patients will do the treadmill, bike, or walk on average 15 minutes per day, they will achieve 80% of the goals of exercise. Relaxation techniques such as biofeedback, deep breathing, and imaging can be helpful for daily headache patients, particularly where stress is a factor. Regarding stress, it is not so much “bad stress”, but “daily hassles” that increase headaches. When patients are faced with overwhelming daily hassles, particularly when they cannot sleep well that night, headaches can be worse the next day.

Psychotherapy is extremely useful for many headache patients with regard to stress management, coping, life issues, family of origin issues, etc. Patients can often learn relaxation techniques from books or tapes that are readily available in bookstores, so that learning relaxation techniques often does not require extended visits to a therapist. If patients are willing and able to see a therapist, I have found that it is much more useful to see a regular psychotherapist about issues and stresses than purely doing biofeedback. However, even though we may recommend psychotherapy, it is crucial to legitimize the headaches as a physical condition; they are <u>not</u> a “psychological” problem, but rather a physical one that stress may exacerbate.

Yoga may be helpful for some headache patients. The idea is to take a class once weekly, and then do the yoga stretches and breathing for 5-10 minutes per day. This may help associated neck or back pain. Physical therapy may also be helpful. Massage may be useful, particularly for the neck pain.

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The following are the general food lists including the sources of caffeine that we have found useful in migraine patients:

Foods to Avoid, and Sources of Caffeine:

You may or may not be sensitive to any of the following foods. If a particular food is going to cause a headache, the headache will usually occur within three hours of eating. Also, the response to the foods may not be consistent. On one occasion, you may have a headache caused by a particular food; however, the next time you eat that same food, it is possible that a headache may not occur.

While foods are <u>not</u> as common a headache trigger as stress, weather, hormones, missing meals, bright lights, and undersleeping, 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 stocks, seasonings, whey protein, soy extract, malt extract, caseinate, barley extract, textured soy protein, chicken or port or beef flavoring, smoke flavor, spices, carrageenan, meat tenderizer, seasoned salt, TV dinners, instant gravies, and some potato chips and dry-roasted nuts.
- Red Wine (White wine is not as likely to trigger a headache)
- Beer
- All alcohol can trigger a headache; beer and wine are the worst offenders
- Chocolate
- Citrus Fruits
- Ripened, aged cheeses (Colby, Roquefort, Brie, Gruyere, cheddar, bleu, brick, mozzarella, Parmesan, boursalt, Romano) and processed cheese.
  - ♦ Less likely to trigger headache: cottage cheese, cream cheese, and American cheese.
- Hot dogs, pepperoni, bologna, salami, sausage, canned or cured meats (bacon, ham), aged meats, or marinated meats.
- Nuts, peanut butter, large amounts of Nutrasweet.
- Yogurt, sour cream.

Caffeine

While caffeine can help headaches, the overuse of caffeine may increase via rebound mechanisms. Some patients do not suffer rebound headaches from the ingestion of 500 mg. of caffeine per day, while others develop rebound headaches with as little as 30 mg. In general, I like to limit caffeine to 150 mg., or at most, 200 mg. per day.

The average 8 ounce cup of coffee has 75 to 125 mg. caffeine. Drip coffee is stronger than percolated, and instant is the weakest form. Depending on the size of the cup and its strength, instant coffee may contain from 40 to 150 mg., but is usually closer to 40 mg. Decaffeinated coffee contains from 2 to 5 mg. per cup. These calculations all depend upon the strength of the product and the brew. Specialty coffeehouses (Starbucks, Caribou, etc.) often contain twice the usual amount of caffeine per cup.

Tea usually contains 30 to 50 mg. of caffeine per cup, and soft drinks average approximately 40 mg.

Chocolate contains 1 to 15 mg. of caffeine per ounce; however, cocoa has considerably more caffeine, up to 50 mg. for an 8 ounce serving.

Caffeine is available in both food products and as tablets or capsules. Caffeine tablets such as NoDoz, Tirend, and Vivarin are available, but I do not use the higher strength products.

When patients find that caffeine significantly decreases their headaches, I will occasionally utilize the pure caffeine tablets, with a dose of 1/2 of a 100 mg. pill (50 mg. total) every 3 to 4 hours as needed. At times, it is helpful to combine the caffeine with medications that do not contain caffeine, such as Midrin.

In whatever form that patients receive caffeine, whether in coffee, caffeine pills, or combination analgesics, it is necessary to limit the total amount of caffeine. 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.

Caffeine Sources

Limit caffeine to 200 mg. per day, or, at most, 300 mg. per day
Coffee: 8 ounces: average cup: 75-125 mg.
drip is stronger than percolated, which is stronger than instant
instant = 40-150 mg. per cup, usually closer to 40 mg.
decaf = 4 mg. per cup
latte = 90 mg
Tea: 8 ounces: average cup: 30-50 mg.
Soft drinks: approximately 40 mg. per cup
Chocolate: 1-15 mg. per ounce
Cocoa - 50 mg. per 8 ounces
Caffeine tablets: (NoDoz, Vivarin, Tirend) = 100 mg. of caffeine
Caffeine is present in many analgesic medications, such as Excedrin Migraine (65 mg.), Anacin (32 mg.) and Vanquish (33 mg.)

Characteristics of Migraine, Chronic Daily, and Cluster Headache

Characteristics of Migraine:
Attacks are 4 to 72 hours
Moderate or moderate-to-severe pain
History by the patient gives the diagnosis, not lab tests
Often early morning, but may be anytime
Unilateral in one half of patients
One to five migraines per month is typical\Gradual onset of pain, a peak for hours, slow decline
Pain is throbbing, pounding, pulsatile, or deep aching
Sharp “ice-pick” jabs are common
Peak ages are between 20 and 35 years
18% of women, 7% of men experience migraine in their lifetime; female/male ratio is 3:1
Family history is often positive for migraine
Associated nausea, photophobia, blurred vision, phonophobia, dizziness is common; however, these may be absent
In women, there is often a positive relationship with menses
Cold hands and feet, or motion sickness is common in migraine patients.

Criteria for Chronic Daily Headache (CDH):

1. Chronic tension headache; more than 4 hours per day, and 15 or more days per month. The chronic daily headaches usually evolve over a period of months or years.
2. Transformed migraine: more than 4 hours per day, and 15 days per month. Previous history of migraine. There is usually a slow increase in tension type headache, with a concomitant decrease in migraine features. No organic causes. Eighty percent of transformed migraine patients have been reported to overuse analgesics. The analgesic abuse may create the daily headaches in some of these patients. Most common reason for daily headache. “Chronic Migraine” is a new term for frequent/daily headaches with migraine features.
3. New daily persistent headache: sudden (over 1 to 3 days) onset of chronic daily headache. No significant previous migraine history, but patients may have had episodic tension headaches in the past.
4. Posttraumatic chronic daily headache: often present with migrainous features. Very difficult to effectively treat. Does not seem to be responsive to the usual medications.
5. Headache associated with cervical spine problems, particularly arthritis: usually posterior occipital. Can be exceedingly difficult to effectively treat.
6. Chronic migraine: CDH that has migraine features (throbbing pain, one-sided, with nausea, sensitivity to light or sound, dizziness).

Links Connecting Tension and Migraine Headache:

Both respond to similar medications: antidepressants and Triptans
Similar serotonergic changes are found in tension and migraine headache patients
Neck pain and muscle spasm are common to both tension and migraine
Family history of headache is present in both migraine and tension headache patients
Prevalence of epilepsy is increased in tension and migraine
Cranial muscle tenderness and cerebral blood flow changes are common to both conditions
Mild migraine is very difficult to clinically distinguish from a severe tension headache
The vast majority of patients with CDH also experience migraine

Typical Characteristics of Patients with Cluster Headache:

Begin between ages 20 and 45, approximately 1 out of 250 men
Male predominance (3:1)
Same time of year, with no headache in between the cluster cycles
Primarily nocturnal attacks
During cluster cycle, alcohol triggers the headaches
Severe, excruciating, unilateral pain, usually periorbital, 45 minutes on average
Ipsilateral rhinorrhea, lacrimation, conjunctival hyperemia, sweating of the forehead, Horner's syndrome
90% of patients have episodic cluster, with breaks between cycles of months.
10% suffer from chronic cluster, with no significant breaks.

Keys to Headache Management

1. Watch headache triggers
2. Treat a migraine early in the headache
3. Do not overuse pain meds/abortives; try and limit to 3 days a week
4. If appropriate, treat with preventative meds
5. Watch sleep and eating, exercise, do yoga or other relaxation techniques.

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Clinical Pearls for Treating Headache Patients

1. Legitimize the headache problem as a physical illness. Statements such as "headaches are just like asthma, diabetes or hypertension: a physical medical condition" go a long way toward establishing trust between the patient and physician. When we mention that it is a medical condition, primarily inherited, and that there is too little serotonin in the brain in people with headaches, patients respond exceedingly well to this. Once we have established this, the patients are much more amenable to addressing anxiety, depression, etc. with therapy or other means. However, if we focus on the patient's stress, anxiety, depression, and psychological comorbidities, they are often turned off to the physician unless we do state that we are treating the headaches as a legitimate medical illness.

2. We must try and achieve a balance between medication and headache; I tell the patients that we are trying to improve the headaches 50% to 90%, while minimizing medications.

3. The initial history and physical is the best time to consider a differential list of medications, because at that point we have a good grasp of the patient's comorbidities. If we list in the chart the other possibilities (in case our initial medications do not work), later we (or our partners) do not have to reconstruct the entire history with the patients.

4. In choosing preventives, look at comorbidities, particularly: anxiety, depression, insomnia, gastritis, GERD, IBS, constipation, hypertension, asthma, and sensitivities or allergies to other drugs. These often determine which way to proceed with medication.

5. Keep track of sensitivities and allergies to medications in a prominent place in the chart. If the patient has had severe reactions to two SSRI's, a third is not a good choice. However, those reactions may not be readily apparent in the chart. If they are extremely fatigued on one ß-blocker, a second will probably not work for the long term.

6. It helps to view chronic headache as a continuum or spectrum. The "in between" headaches may not fall neatly into the current tension or migraine categories. Whether these are severe tension or milder migraines, they often respond to the same medications.

7. Start with low doses of medication, particularly with antidepressants and other preventives. Headache patients tend to be fairly somatic, and there is no need to push medicine very quickly. One exception to this is in patients with severe "new onset daily persistent headache"; these patients may be less patient.

8. Keep a drug medication flow chart. Headache patients are constantly having medications stopped and re-started, and over ten years, a patient may have been on 50 different medications at various times. It is impossible to piece through forty progress notes trying to determine what the next best course of action is. A drug medication flow chart from the beginning helps immensely.

9. When we place patients on antidepressants, we need to make it clear that we are trying to directly help their headache by increasing serotonin. We also state that we certainly hope this helps anxiety, depression, etc. Patients are often confused as to the reason why they are given an antidepressant. It helps if we make it clear that we are not trying to treat their headache by treating depression.

10. Watch for soft bipolar signs in headache patients who have anxiety and depression. Bipolar disorder tends to be underdiagnosed, and the clinical stakes for missing it are enormous. Bipolar disorder, primarily mild and soft (Bipolar II or III), is seen in as many as 6% to 7% of migraineurs. While many of these patients will do well on an antidepressant, it is often necessary to add a mood stabilizer (Depakote, lithium).

11. Many patients are frustrated by the lack of efficacy and/or side effects of daily preventives. Tell them that only 50% (at most) of patients achieve long-term relief with preventives. This helps them to realize they are in a big boat, and that it is not their fault.

12. We need to stick with preventive medications for at least four weeks (or longer); if we abandon them too soon, we may not see the beneficial effect. However, few patients are willing to wait months for positive benefits from a medication.

13. We cannot promise patients that their headaches will improve with psychotherapy (as it often does not), but coping with headaches and the stresses that headaches produce is often improved with therapy. Unfortunately, because of stigma, time and money, only a small minority of patients will actually go to a therapist. However, those that do go will usually benefit.

14. Patients with chronic daily headache may view the headache situation in black and white terms; they will come back for a return visit and state, “Well, I still have a headache everyday.” They need to accept that if we have gone from moderate to severe headaches (7 on a scale of 1-10) to mild to moderate (4 on a scale of 1-10), that the situation is improved and we should not change all the medication. If the patients keep a headache chart or calendar, this may help. Patients need to be willing to accept 50% to 90% improvement in frequency and/or severity.

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15. While most patients are honest about analgesic use, some are embarrassed to tell us how much they are utilizing. Between OTC analgesics and herbal preparations, many patients are consuming larger quantities of medications than we realize.

16. Weight gain is a major issue; even though a drug may be more effective, choosing one that avoids weight gain (in those prone to it) is more likely to lead to long term success. Fatigue is another major reason for patients abandoning a preventive medication. Headache patients commonly complain of fatigue.

17. Do not confuse addiction with dependency; when treating chronic daily headache, dependency has to be accepted. Unfortunately, DSM-IV is inadequate in addressing prescription abuse.

18. What to do when nothing works: Before "giving up" on a patient with severe, refractive chronic daily headache, consider "end of the line" strategies such as: MAOI's, daily long-acting opioids (methadone, Kadian, Oxycontin, MS-Contin), stimulants (dextroamphetamine, methylphenidate, phentermine), IV DHE, daily triptans in limited amounts, Botox injections, or combinations of approaches.

19. Using a medication to establish a diagnosis may not be accurate. For instance, DHE or triptans have been effective for the pain of SAH or tumors.

20. Acceptance of the chronic illness (headache) is a helpful state of mind for patients to achieve. Acceptance is different than resignation. Acceptance helps to ease anxiety ("isn't there a cure; these must be curable"). The road to acceptance may take years, and involve many doctors and alternatives.

21. When patients feel that they can actively help their headaches ("self-efficacy"), by medication or biofeedback or other means, it improves their sense of well-being. Whether by taking a medication, watching triggers, exercising, or doing Yoga, etc., increasing "self-efficacy" enhances outcomes.

First Line Migraine Abortive Medications

Triptans

1. 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 (6 mg.) Imitrex is the most effective migraine abortive for more severe, faster onset migraines. The addition of an nsaid to a triptan may enhance efficacy, and prevent headache recurrence. Also available as a nasal spray. Over 50 million people have had Imitrex, and it has been utilized for 15 years. It is highly effective.

2. Relpax is an effective and well-tolerated triptan. It is available in 20 and 40 mg. strengths. The side effects have, in general, been found to be fairly minimal. These include possible nausea, pressure in the throat, dizziness and tiredness or weakness. Although chest pressure/pain/tightness may occur with Relpax, these symptoms have not been seen very often (only 1 to 2% of patients). In long-term studies, only 8.3% of patients discontinued the Relpax due to side effects. There have been excellent cardiac safety studies. Avoid with 3A4 inhibitors.

3. Zomig: Zomig, 2.5 mg. or 5 mg., is another in the growing list of triptans. 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. Zomig has the same general tolerability and efficacy profile as the others. Again, if patients do not tolerate one triptan, it is often worthwhile to try another because they may be able to tolerate another version. Zomig nasal spray is fast-acting and very effective.

4. Axert: Very similar to the other triptans, effective for migraine headache. The usual dose is one 12.5 mg. tablet, every 3 to 4 hours, 2 per day only. Side effects are similar to those of the other triptans; Axert is very well tolerated. Axert is able to combine good efficacy with excellent tolerability.

5. Maxalt: Very similar to Imitrex. Maxalt is very effective for migraine. The usual dose is one 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. Side effects are similar to those of Imitrex. Maxalt is very well tolerated. Certain patients tolerate one of these triptans better than another and it is worthwhile to try several in an individual patient. While some patients utilize the 5 mg. tablet, 10 mg. is well tolerated and more effective. The MLT form may be taken without water, which is an advantage.

6. Amerge: The usual dose is 2.5 mg. every three to four hours as needed, two or three in a day at most. Amerge is the “kinder, gentler, smoother” triptan. Amerge takes longer to work, up to two hours, but has a long half-life. With a half or one tablet of Amerge, most patients will not have more than minimal side effects. It is better tolerated that the other triptans, but somewhat less effective than Imitrex. Amerge is good for long lasting headaches or headaches of slow, rambling onset. Amerge can also be used as a preventive medication for menstrual migraine. If triptans are used as preventive medications, Amerge may be a good choice.

7. 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.

Non-Triptan First Line Abortives

1. Migranal Nasal Spray: Migranal Nasal Spray is dihydroergotamine (DHE). This has been available since 1945 in one form or another with remarkably few serious side effects in all of that time. The usual dose is one spray in each nostril and you can repeat it, and often do need to repeat it, in 15 or 20 minutes. That would be the maximum for the day, which is two sprays in each nostril. Migranal is relatively well tolerated. As with the triptans, tightness in muscles, a flushing feeling, or slight chest heaviness can occur. Nasal stuffiness is relatively common with Migranal. Since DHE is primarily a venoconstrictor and is only a mild arterial constrictor, Migranal may be safer in the population with risk factors for cardiac disease. Migranal may also be useful for menstrual migraines, as it has a fairly long duration of action. Not quite as effective as triptans.

2. Excedrin (Excedrin Migraine): Useful as an over-the-counter preparation with 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 3 hours as needed are effective for many patients with mild or moderate migraines. Tension Excedrin is also available, but is less effective. This contains acetaminophen plus caffeine. Rebound may occur with overuse; 4 per day (and not on a daily basis) should be the maximum.

3. Naproxen (Anaprox, Naprelan, Aleve): Useful in younger patients, occasionally helpful for menstrual migraine. Naprelan is an outstanding long-acting form of Naproxen, available in 375 mg. and 500 mg. Nonsedating, but very frequent GI upset. The usual dose is 500 mg. with food or Tums to start, then may repeat in one hour (if no severe nausea), and then in 3 or 4 hours. Three per day at most. OTC as Aleve, 220 mg., and generic is available. Adding caffeine increases efficacy. Naproxen may be used at the same time as a triptan. Bextra, Celebrex (COX-2 inhibitors) or other nsaids may be used.

4. Ibuprofen: Over-the-counter, and approved for children. Liquid Advil is available. Not as effective as Anaprox. Occasionally useful in 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 with caffeine may be helpful. The short half-life is a drawback. May be used with triptans, even at the same time.

5. Midrin. Effective, safe and used in children. Fatigue is common. Contains a vasoconstrictor, a nonaddicting sedative, and acetaminophen. Usual dose is one or two caps to start, then one every hour as needed, five or six per day at most. May be combined with caffeine for increased efficacy. Generally well tolerated. Generic may not work as well. After many years, remains an outstanding abortive, but not as effective as triptans.

Second Line Abortive Migraine Medications

1. Ketorolac (Toradol): The injections are much more effective than the tablets. Patients may use the injections, 60 mg. per 2 cc at home. The syringes have changed, where Toradol is now available in vials, which the patient must draw up into the syringe. These have the advantage over the pre-filled syringes in that we can use a smaller gauge and shorter needle than was previously available. The usual dose is 60 mg., which may be repeated in 1 hour if necessary. Nausea or GI pain may occur. Ketorolac is nonaddicting and does not usually cause sedation. Limit to 3 per week due to possible nephrotoxicity. Generic is available. IV Toradol is very effective.

2. DHE Injections: Effective as an IV or IM injection, and occasionally as a nasal spray. DHE is safe and well tolerated. Nausea, leg cramps, and burning at the injection side 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. Migranal is the brand name of DHE Nasal Spray.

3. Fiorinal, Fioricet, Esgic, Phrenilin: (see section on Butalbital Compounds for ingredients of these compounds). Fiorinal contains ASA, butalbital, and caffeine; Fioricet, Phrenilin and Esgic replace the ASA with acetaminophen. Generics of these compounds do not work well. These are addicting, but very effective for many patients. Dosage is one or two tablets or capsules every 3 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, spaciness, or euphoria are common.

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4. Narcotics: Fiorinal with codeine, Vicoprofen, Vicodin, oxycodone, meperidine, etc. PO or IM, these are often the best of the 'last resort' approaches. 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 is a milder, newer analgesic, with relatively few side effects. Vicoprofen combines 7.5 mg. of hydrocodone with 200 mg. ibuprofen; 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.

5. 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, ½ or 1 every 4 to 6 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, fatigue 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.

6. Ergots: Vasoconstrictors, with many side effects, but usually effective. Nausea and anxiety are common with ergotamine compounds. Cafergot adds caffeine to the ergotamine. Only generic Cafergot PB is available. Suppositories are more effective than 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.

7. 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 newer "atypical antipsychotics", such as Zyprexa or Seroquel, may be occasionally useful on a prn basis. In the ER, IV Compazine or Reglan may be useful.

Antiemetic Medication

1. Promethazine (Phenergan): Mild but effective for most patients. Very sedating. Low incidence of extrapyramidal side effects. Available as tablets, suppositories and oral lozenges (formulated by compounding pharmacists). Used for children and adults.

2. Prochlorperazine (Compazine): Very effective but 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.

3. Metoclopramide (Reglan): Mild, but well tolerated, commonly used prior to IV DHE. Fatigue or anxiety occur but are not usually severe. Five to 10 mg. are given PO, IM or IV.

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

5. Chlorpromazine (Thorazine): Extremely effective but with increased side effects, particularly sedation. The suppositories often prevent an ER trip by sedating the patient and stopping the nausea. Used with patients where other antiemetics have failed.

6. Zofran: 4 or 8 mg. PO, very effective with few side effects. Very expensive. Not sedating. Zofran is extremely useful for patients who need to keep functioning and not be sedated with an antiemetic. Most patients who use Zofran also utilize another less expensive antiemetic for other times. Available as oral tablets or as Zofran ODT, orally disintegrating tablets.

Information that Patients Need to Know Prior to Starting Prevention Medication

1. The realistic goals of the medications are to decrease the tension headache severity by 70%, not to completely eliminate the headaches. It is always wonderful when the headaches are 90% to 100% improved, but the idea is to minimize medication. Most patients need to be willing to settle for moderate improvement.

2. Patients must be willing to change medication, if necessary. They need to know that what is effective for someone else may not work for them. Trial and error may be needed to find the best preventive approach for that person.

3. The preventive medications may take weeks to become effective. The doses often need to be adjusted, and thus patience will be necessary with these medications. The physician needs to be available for phone consultations pertaining to the headaches and medicine.

4. Most preventive medications are utilized in medicine for another purpose. It is best if patients are informed, for instance, that Elavil is also used for depression, usually in much higher doses. Patients should be told why we are utilizing Evavil, and that it is not because they are depressed.

5. Side effects are possible with any medication, and the patient has to be prepared to endure mild side effects in order to achieve results. We cannot simply stop medication and switch to another because of very mild side effects. Most patients are willing to put up with mild, annoying side effects.

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6. In the long run, preventive medications are only effective for approximately 50% of patients.

7. Preventive medications are individualized toward the patient's needs. We use a particular preventive depending upon the person's comorbidities, GI system, medication sensitivities, etc.

First Line Preventative Medications for Migraine

Patients with more than 3 migraines per month, that are not well controlled, may be candidates for preventatives. Those with CDH may be more likely to need preventatives. We choose a preventative based upon headaches and comorbidities (anxiety, depression, GI, etc.)

1. Valproate (Depakote): This seizure medication is becoming increasingly popular for migraine prevention. Usually well tolerated in the lower doses utilized for headaches. 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. 250 ER is also available. Should not be used during pregnancy. As with most preventives, Depakote may not become effective prior to 4 or 6 weeks. Along with Topamax, it is FDA approved for migraine prevention.

2. Topamax (topiramate): Topamax is FDA approved as a migraine preventive. This anti-seizure medication has been 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 use. Topamax often decreases appetite, which leads to weight loss; this is unusual among headache preventatives. 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. Acute glaucoma has been a rare side effect. GI upset may occur. The risk of forming kidney stones is increased by the use of Topamax. Bicarbonate levels should be monitored, as Topamax may cause a dose-related metabolic acidosis.

3. Beta Blockers: Effective. Long-acting (LA) Inderal capsules may be dosed once per day. Occasionally effective for daily headaches. Sedation, diarrhea, lower GI upset and weight gain are common. Very useful in combination with amitriptyline. Dosage begins with LA 60 mg., and is usually kept between 60 and 160 mg. per day. Other ß-blockers also are 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 less respiratory effects.

4. Amitriptyline (Elavil): 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 generally used more for daily tension-type headaches. Protriptyline is one of the only older antidepressants that does not cause weight gain. However, anticholinergic side effects are increased with protriptyline. While the SSRI's are utilized, they are probably more effective for anxiety, depression, and CDH than for migraine.

5. Naproxen (Naprosyn, Naprelan, Anaprox, Aleve): Useful in younger patients, once a day dosing. Sometimes helpful for daily headaches. Particularly useful for menstrual migraine. Nonsedating, but frequent GI upset. Effective as an abortive, and 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. OTC as Aleve. Other anti-inflammatories can be utilized for prevention of migraine. As with all anti-inflammatories, GI side effects increase as people age, and so we use these much more in the younger population.

6. 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. May be combined with other first line medications, particularly amitriptyline or naproxen. Constipation is common. Starting dose is ½ 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 120 mg. or 180 mg. per day. Verelan is a useful brand name.

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Second Line Migraine Preventative Therapy

1. Neurontin (gabapentin): An anti-seizure medication that has been demonstrated to be useful in migraine and tension headache prophylaxis. Doses are available in 100 mg., 300 mg., 400 mg., 600 mg. and 800 mg. sizes. The usual dose for headache prevention is 600 to 2400 mg. per day. In a large study on migraine, doses ranged around 2,300 mg. per day. Sedation and dizziness may be a problem; however, Neurontin does not appear to cause end-organ damage, and weight gain is relatively minimal. Neurontin can be used as an adjunct to other first line preventive medications. Some patients do well with very low doses (200 or 300 mg. per day).

2. 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 ß-blocker. This combination is commonly used for "mixed" headaches (migraine plus chronic daily headaches). 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 (i.e., anxiety, depression, etc.) are present.

3. Zanaflex (tizanidine): A safe, non-addicting muscle relaxant, Zanaflex 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 ¼ or ½ tablet. Sedation and dry mouth are common. Zanaflex may be used on a prn basis for milder headaches, or for neck or back pain. A 2 mg. tablet is also available. Generic is available.

Preventative Medication: When to Proceed Quickly with Two Preventives at One Time

1. With most patients, we utilize one prevention medication at a time, in low doses, slowly raising the dose as needed. Most of the patients appreciate the approach, and are perfectly willing to wait for the medication to work.

2. At times, patients may become extremely frustrated with the headaches, and they desire quick results. When these patients suffer from moderate or severe CDH, with bothersome migraines, it is justified to push ahead at a faster rate with a preventive approach. For instance, amitriptyline and verapamil, or amitriptyline and propranolol may be initiated at the same time. Alternatively, doses may be increased very quickly. The IV DHE repetitive protocol may be utilized, with one or two preventive medications instituted concurrently. The initial amount of preventive medication utilized for a patient depends upon the severity of the headaches and the frustration level of the patient.

3. Patients with new onset of severe headaches, which are usually daily headaches plus migraine, are often extremely upset and frustrated with the pain. In this situation, pushing preventive medication at a faster pace is justified.

Third Line Migraine Prevention (For Refractory Patients)

1. Long-acting opioids (methadone, Oxycontin, Kadian, MS-Contin, Avinza, Duragesic): In a very small select group of severe headache patients, particularly with severe, refractive, chronic daily headaches and migraines, long-acting opioids have some demonstrated utility. Methadone may work because of its antagonism on NMDA. Methadone is relatively well-tolerated, but sedation and constipation are limiting factors. Doses need to be kept low, from 5 mg. to 20 mg. per day. Morphine is available in multiple forms. Kadian is usually dosed at 20 mg. once or twice daily; it is remarkably smooth and long-acting. Avinza is a good once-daily morphine. Oxycontin is a long-acting oxycodone without the acetaminophen or aspirin. Oxycontin can also be useful, but may be more prone to abuse, and only lasts 5 to 8 hours in most patients. The Duragesic patch lasts 72 hours. Opioids may be combined (in low doses) with stimulants. Stimulants may help the pain, and also offset fatigue. Patients must accept the risks of these medications.

2. Repetitive IV DHE Therapy: Helpful for patients with frequent migraine, severe daily headache, and status migraine. Weeks of headache improvement are often seen. IV DHE is useful in patients withdrawing from analgesics. The protocol can be done in the office or hospital. In the office, the first dose, 1/3 mg. is given, and if it is well tolerated, the subsequent doses are ½ or 1 mg. Oral Reglan is usually given prior to the DHE. Three or four doses are given in the office, and up to nine in the hospital. Side effects include nausea, heat flashes, muscle contraction headache, leg cramps, diarrhea, and GI pain. The

IV DHE is usually well tolerated and effective. After the DHE, patients are continued on prevention medication. Occasionally, Migranal (DHE) nasal spray, used daily for several weeks, is also effective.

3. Stimulants: (Dextroamphetamine, Methylphenidate, Phentermine, Adderall): Occasionally useful as a "last resort" therapy. These also offset fatigue. Phentermine is also a possibility and can be used as an adjunct to other medications. Phentermine is activating and can cause insomnia. However, it can also help decrease appetite, which is its primary use, and decreases sedation in patients with chronic fatigue. Dexedrine and Ritalin (or Concerta) may be used in combination with long-acting opioids. Adderall is also a useful, longer-acting compound. Adderall XR is a good, once-daily form. Addiction is always a risk with the use of stimulants. Fatigue is a common problem for headache patients, and stimulants may help.

4. Phenelzine (Nardil): This MAO inhibitor (MAOI) is a powerful migraine and daily headache preventive medication. Phenelzine is very helpful for depression, anxiety and panic attacks. The risk of a hypertensive crisis is small, but is a major drawback to the MAOIs. Dietary restrictions render MAOIs difficult for the patient. Side effects include insomnia and weight gain, both of which are often major problems. Dry mouth, fatigue, constipation and cognitive effects may also occur. Patients need to be aware of the symptoms of hypertensive reactions. The usual dose is 45 mg. each night (3 of the 15 mg. tablets). This is adjusted up or down, and the range varies from one to five tablets per day. One other major drawback is that certain triptans cannot be used with MAOIs.

5. Frequent Triptans: In some patients with chronic daily headache and frequent migraines, or "chronic migraine", the only medication that is useful is a low dose triptan. Long-term side effects are unknown at this time, and this needs to be understood by the patient. Rebound headache needs to be excluded in these patients.

6. Botulinum Toxin Injections: Botulinum Toxin A (Botox) has been extensively studied in migraineurs. Approximately 50 to 60% of patients have significant relief after Botox injections; low doses, primarily frontal and temporal, are usually used (50 to 100 units total per patient, in 8 to 12 injections). While expensive, Botox is relatively safe and only takes a few minutes to inject. One set of injections can decrease the headaches for 1 to 3 months. The role of botulinum toxin will become more clear in the next 5 years. Posterior (occipital), or upper cervical injections are just starting to be investigated, and appear to have some utility. Botulinum toxin may be safer than many of the medications that are utilized.

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“Natural” Headache Herbs/Supplements

Feverfew, petadolex, magnesium oxide, and Vitamin B2 have all held up in double-blind studies as migraine preventatives.

1. Feverfew: Feverfew has been demonstrated to be effective in some patients for prevention of migraine headache. Feverfew can cause a mild increased tendency toward bleeding, and should be discontinued 2 weeks prior to surgery. Feverfew should not be used during pregnancy. Patients occasionally will be allergic to feverfew. The problem with many herbal supplements is quality control, and certain farms consistently have better quality than others. The parthenolide content (the active ingredient) varies widely from farm to farm. The usual dose is 2 capsules each morning. Eclectic Institute (a blue and white bottle, widely available in health food stores and Whole Foods) freeze dries their herbs, and the product is highly consistent and reliable.

2. Magnesium Oxide: It has been shown that magnesium levels are low in the brain of migraine patients. 400 or 500 mg. per day as a preventive; however, GI side effects may limit use. Mag Ox (400 mg.) is a good brand that is well absorbed. 250 mg. tablets are found in most pharmacies.

3. Petadolex: Commonly used in Europe, this herb has held up in several well-designed blinded studies. The usual dose is 3 per day. Earlier concerns about carcinogenisis with this family of herbs have decreased with petadolex. It is prudent to stop it every 3 months or so. Available at 1-888-301-1084.

4. Long Chain Fatty Acids (Omega-3, Omega-6 fatty acids): These may play a role in headache prevention, as well as (possibly) useful for anxiety, HTN, arthritis, high lipids, depression and heart disease. We usually recommend Flaxseed oil, 1000 mg., 2 or 4 per day (in studies on depression, 8 per day have been utilized). Fish oil capsules may be more effective than Flaxseed oil. Grapeseed and safflower oil contain Omega-6’s. Oily, fatty fishes (Salmon, Tuna) contain more than other fishes.

5. Vitamin B2: 400 mg. per day has been utilized in at least two blinded studies, with effect on milder migraines. B6 and B12 may also play a preventive role. Long-term side effects of B2 in larger doses are not known.

6. Coenzyme Q-10: COQ-10 is relatively safe, and has started to be investigated as a headache preventive. Doses for headache are not known. COQ-10 may have some positive effects on the heart as well. We usually recommend 150 to 300 mg. daily.

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Treatment of Menstrual Migraine

Menstrual headaches are often severe, prolonged and debilitating. The abortive therapy follows the general abortive therapy for migraine. (See abortive therapy section.) In addition to the usual abortives, cortisone (Prednisone, Decadron) is effective for many women; it is utilized in very limited amounts. The severe intensity of menstrual migraines often dictates stronger abortive measures. Triptans are particularly useful. Many women with severe menstrual migraines require combinations of triptans, low dose cortisone, analgesics, and antiemetics.

Preventive Treatment: The timing of preventive therapy is difficult for most women; either their menstrual periods are irregular, or the headaches occur at different times. However, in some women the following may be helpful:

1. NSAIDs (Naproxen, etc.): Effective for many women and usually well tolerated. These are started 3 days prior to the expected onset of the headache. Many NSAIDs have been utilized, including naproxen, ibuprofen, flurbiprofen, meclofenamate sodium, etc. GI upset is common. Bextra or Celebrex may also be useful.

2. Triptans: Amerge (naratriptan) is a long-acting, smooth, well-tolerated triptan. Its utility in menstrual migraine has been established. One method of dosing it is 2.5 mg. once or twice a day for three to five days around the time that the menstrual migraine would occur. Frova is also effective. While not as well studied, the other triptans may also be helpful as menstrual migraine preventives.

3. Hormonal approaches: Estrogen has been used, but is questionably effective. Occasionally, the birth control pill, even on a cyclic basis, will reduce headaches. If used continuously (no break), it may provide some relief. The birth control pill, however, can also increase migraines. As with other preventives, hormonal approaches often are disappointing, or they may initially provide relief, with declining efficacy over months.

First Line Tension Headache Abortive Medications

1. Acetaminophen, Aspirin: These are the staple of OTC pain relief; acetaminophen is less effective for headache, but better tolerated. These need to be limited, so as to avoid the rebound situation.

2. Ibuprofen (Motrin, Advil, Nuprin): Helpful for migraine and tension headache. Useful in children, and a liquid form is available. GI upset is relatively common, but ibuprofen is more effective for headache than acetaminophen. Adding caffeine can increase efficacy.

3. Caffeine: Caffeine beverages or tablets (100 mg.) are helpful for migraine and tension headache, either alone or as an adjunct to analgesics. Caffeine added to other abortives enhances their effectiveness and decreases drowsiness.

For example, Midrin plus caffeine is an effective combination. Caffeine must be limited so as to avoid “rebound” headaches. The usual limit should be 150 or 200 mg., at most, in one day.

4. Caffeine-aspirin combinations: Excedrin Migraine has 65 mg. caffeine, 250 mg. of aspirin, and 250 mg. of acetaminophen; this is a very effective OTC preparation, but overuse leads to rebound headaches. Anacin contains much less caffeine (32 mg.), but more aspirin. Tension Excedrin is a very useful combination of acetaminophen and caffeine. Norgesic Forte is a very useful combination of aspirin, caffeine, and orphenadrine (a non-addicting muscle relaxant; generic is available).

5. Naproxen (Anaprox, Aleve (OTC), Naprelan): Useful in younger patients, nonsedating, but very frequent GI upset. The usual dose is one 500 mg. tablet with food, which may be repeated up to a maximum of three per day. If used on a daily basis, two per day should be the limit. Adding caffeine can increase efficacy. Naprelan is an excellent long-acting form of naproxen, available in 375 mg. and 500 mg. One Aleve=220 mg. Also available as generic naproxen OTC (220 mg.).

6. Cox-2 inhibitors (Celebrex, Bextra): These are useful for some headache patients, with less GI side effects. Adding in caffeine may enhance efficacy. The usual dose of Celebrex is 200 mg. once or twice daily, “as needed”. Bextra is dosed at 10 or 20 mg. prn, 40 mg. in a day at most. Long-term safety of daily use is unknown.

7. Midrin (generic available): Effective, safe, and used in children as well as adults. Primarily a migraine abortive, Midrin is also very helpful for tension headache. The usual dose is one or two per day to start, then one every hour as needed, five or six per day at most. May be combined with caffeine for increased efficacy. Sedation and light-headedness may occur. May also be combined with nsaids. Midrin is now a Schedule 4 drug.

8. Tramadol (Ultram): 50 mg. tablets, 1 or 2 every four hours, relatively few side effects but sedation, nausea, and dizziness may occur. Addiction uncommon but is occasionally seen. Need to limit to 4 per day, 10 per week. Generally well tolerated. Ultram is an “opioid-like” medication that is milder than codeine or hydrocodone. Overuse may lead to seizures.

9. Ultracet (37.5 mg. Tramadol, 325 mg. Acetaminophen): A milder, somewhat effective analgesic. Need to limit to 4 per day, 10 per week. *See Tramadol above*.

10. Ketoprofen: NSAID now available OTC. Most patients require 3 or 4 of the low strength OTC tablets. Adding caffeine can increase efficacy. Same GI side effects as with other NSAIDs.

Second Line Tension Headache Abortive Medications

1. Butalbital compounds: Effective but habit forming. Fiorinal, Esgic, Esgic Plus, Fioricet, and Phrenilin are the primary butalbital compounds. Generic butalbital preparations do not work as well as brand names. Sedation or euphoria is common. Strict limits need to be set for daily and monthly use. If used daily, one or two is the usual limit. These should not be used daily unless preventive medications, and milder abortives, have failed.

See “Butalbital (Fiorinal) Compounds” for ingredients of butalbital compounds.

2. Narcotics: Codeine, hydrocodone, and propoxyphene are a last resort, and should be limited per month, and generally should not be used on a daily basis. These need to be discontinued if patients use them to alleviate stress, depression, fatigue or anxiety. Vicoprofen (generic available) combines 200 mg. ibuprofen with 7.5 mg. hydrocodone, and is generally more effective than Vicodin. Rebound and addiction are always a primary concern.

3. Sedatives: Most are benzodiazepines, such as diazepam (Valium) and clonazepam (Klonopin). Sedation is common. Because they are habit forming, these need to be monitored with a monthly limit. They are a last resort, not a first choice. Addiction is always the major drawback.

4. Triptans: While triptans are generally utilized for migraine and cluster headaches, the triptans can be useful for tension headaches as well, particularly the more severe tension headaches. There are some patients who only do well with a triptan with any of their headaches. In migraine patients, triptans often work for their “lesser” headaches.

5. Muscle Relaxants: These are occasionally useful on a “prn” basis; the non-addicting ones are preferred. These include orphenadrine (Norflex), tizanidine (Zanaflex), cyclobenzaprine (Flexeril), and Skelaxin. These may be combined with caffeine or nsaids. Sedation may be a problem. Zanaflex, ¼, ½ or 1 of the 4 mg. tablets, is particularly useful. Skelaxin is mild but nonsedating. Norgesic Forte combines aspirin, caffeine, and orphenadrine; the usual dose is ½ or 1 every 4 hours prn, 2 in a day at most.

Butalbital (Fiorinal) Compounds

(Generic generally not as effective)

Drug	Dose	Comment
Fiorinal Butalbital 50 mg. Aspirin 325 mg. Caffeine 40 mg.	1 or 2 every 3 hours PRN; 6 a day maximum	Habit forming; the aspirin may cause nausea. The most effective of the butalbital class.
Fioricet or Esgic Butalbital 50 mg. Acetaminophen 325 mg. Caffeine 40 mg. Esgic Plus has 500 mg. of acetaminophen	1 or 2 every 3 hours PRN; 6 a day maximum	Less nausea than with fiorinal, but less effective, because acetaminophen not as effective as aspirin
Phrenilin Butalbital 50 mg. Acetaminophen 325 mg. Phrenilin Forte has 650 mg. of acetaminophen	1 or 2 every 3 hours PRN; 6 a day maximum	Less effective than the other butalbitals; good for use at night (no caffeine), less nausea.
Fiorinal with codeine (30 mg.) Fioricet with codeine (30 mg.)	1 every 3 hours PRN; 4 a day maximum	The codeine helps but increases the side effects (nausea).

First Line Chronic Daily Headache (CDH) Prevention Medication

1. Valproate (Depakote): See “First Line Preventative Medications for Migraine”

2. Amitriptyline (Elavil): See “First Line Preventative Medications for Migraine”

3. Topamax: See “First Line Preventive Medications for Migraine”.

4. SSRI’s and Effexor: Fewer side effects than amitriptyline, but not as effective. More effective for anxiety and depression than for headache. Nausea, anxiety, sexual dysfunction, fatigue, and insomnia are common. Weight gain is relatively common. Helpful for migraine in some patients. Begin with low doses. All of the SSRI’s have been somewhat useful for preventing chronic daily headache, and to a lesser extent for migraine. The dose for headache is usually lower than that for depression. Considering tolerability, these are often the best choice for chronic daily headache. Any of these may also exacerbate headaches. See antidepressant section.

5. Protriptyline (Vivactil): Effective and nonsedating. Weight gain does not occur. Dry mouth, constipation, dizziness are common. Used in the morning, as insomnia may occur. May be used in the morning with a sedating tricyclic at night. Usual dose is 5 to 15 mg. per day (lower than for depression). The only tricyclic that tends not to cause weight gain.

6. Nortriptyline (Pamelor): A metabolite of amitriptyline. Better tolerated than amitriptyline, but less effective. Side effects are similar to amitriptyline, but less

severe. Useful in children, adolescents and the elderly. Occasionally helpful in migraine. Usual dose is 25 to 75 mg. per day; some patients do well on one 10 mg. daily.

7. Doxepin (Sinequan): Very similar to amitriptyline. Begin with very low doses (10 mg. each night), as many patients cannot tolerate more than this amount. Usual dose is 25 to 75 mg. per day. Same side effects as amitriptyline, but generally better tolerated.

8. NSAID's: Not as effective as antidepressants for chronic daily headache, but without the cognitive side effects. GI side effects are common, however. Hepatic and renal blood tests need to be monitored. NSAID's are used more frequently in younger patients. Ibuprofen is available over the counter, but is short-acting. Naproxen (Naprosyn, Naprelan, Aleve, Anaprox) is more effective than ibuprofen. Flurbiprofen (Ansaid), diclofenac sodium (Voltaren), and ketoprofen (Orudis, Oruvail) are also utilized. As always, attempt to use the minimum effective dose. See previous NSAID sections.

9. Neurontin: See "First Line Preventative Medications for Migraine"

10. Zanaflex: See "Second Line Migraine Preventative Therapy"

Second Line CDH Preventative Medication

1. ß-blockers: Occasionally useful for daily headache and very effective for migraine. See "First Line Preventative Medications for Migraine"

2. Muscle relaxants: Safe but only mildly effective; some patients do respond well to these. Fatigue is a prominent side effect. See "Second Line Tension Headache Abortive Medications"

3. Calcium channel antagonists (Verapamil): Occasionally effective for daily headache as well as migraine and cluster. Verapamil is the most widely used calcium blocker. See "First Line Preventive Medications for Migraine"

Third Line CDH Preventative Therapy

1. Polypharmacy: Combinations of two of the first or second line preventives are often very effective. Tricyclics or SSRI's may be combined with NSAIDs or ß-blockers; NSAIDs may also be combined with ß-blockers or verapamil. Valproate (Depakote) may be combined with tricyclics, ß-blockers, or

verapamil. Topamax may be combined with certain meds. The various preventive medications possess different mechanisms of action.

2. Long-acting Opioids: See “Third Line Migraine Prevention”.

3. Repetitive IV DHE: Four to nine injections of DHE are utilized over 2 to 4 days, either in the hospital or, preferably, as an outpatient. More effective for migraine, but daily headache often responds to DHE. See “Third Line Migraine Prevention”. DHE has become much more expensive.

4. Tranquilizers: More useful in patients with severe anxiety disorders. Occasionally effective for daily headache, but habit forming. Benzodiazepines are the primary sedatives used for daily headache. Doses need to be minimized and patients must be carefully monitored. Alprazolam (Xanax), Clonazepam (Klonopin), and diazepam (Valium) are the usual benzodiazepines that are used.

5. Stimulants: Helpful for some patients as an “end of the line therapy”. See “Third Line Migraine Prevention”. These may offset the fatigue so commonly seen in headache patients.

6. MAO inhibitors (phenelzine): Phenelzine (Nardil) is a powerful antidepressant for migraine and daily headache. See “Third Line Migraine Prevention”. There are significant risks and side effects.

7. Daily Triptans: See “Third Line Migraine Prevention”.

8. Botulinum Toxin injections: These are not as useful for CDH as for migraine. Studies in CDH patients have resulted in mixed results. However, in certain patients these do decrease the daily headaches. See “Third Line Migraine Prevention”.

First Line Abortive Medications for Cluster Headache

1. Oxygen: Very effective, with no side effects. May be combined with other abortives. Oxygen is worth trying for all patients willing to rent a tank; the usual dose is 8 liters/min., for 10 to 20 minutes as needed, with a mask, used sitting up and leaning slightly forward. 60% success rate.

2. Sumatriptan (Imitrex) injection: The most effective cluster headache abortive medication. The injections often work within minutes, and cluster patients often prefer this route of administration. However, patients may at times require two or three injections in a day. Chest heaviness or pressure, tingling or hot sensation, nausea, fatigue, etc. may occur. Many cluster patients do well with 3 mg. sq of the injections; for ½ doses (3 mg.), the individual vials are ordered, with insulin syringes.

3. Sumatriptan (Imitrex) nasal spray: The 20 mg. nasal spray is convenient and easy to use. While not as effective or as fact acting as the injection, many patients do prefer this route. Side effects tend to be minimal, but an unpleasant taste in the mouth is common. Cluster patients often require two or three nasal sprays in a day. Many patients utilize nasal spray at times, and the injections at other times. Occasionally, the tablets of triptans are preferred by cluster patients. Zomig NS is newer and is effective for some cluster patients.

4. Oral Triptans: Most tablets (including dissolving tabs) have been used for clusters; these are more helpful for longer clusters, or clusters that are more moderate in intensity. See section on Migraine Abortive Medications.

Quick Reference Guide: First Line Cluster Preventative Medication

1. Cortisone: Very effective for cluster headache; is used primarily for episodic clusters. It is given for 1 or 2 weeks during the peak of the cluster series. Prednisone, Decadron, or injectable forms may be utilized. When used for short periods of time, side effects are minimal. A typical regimen is prednisone (20 mg.) or Decadron (4 mg.) once a day for 3 days, then one-half tablet per day for 10 days, then stop. Additional cortisone may be given later in the cycle, when the clusters increase. Higher doses may be needed, particularly when the cluster cycle is peaking in intensity. Due to adverse events, it is very important to minimize the cortisone.

2. Verapamil (Covera HS, Calan, Isoptin, Verelan): A well tolerated calcium channel blocker; effective in episodic and chronic cluster. One 240 mg. ER tablet is taken once or twice per day. This is often initiated at the onset of the headaches, in conjunction with cortisone. Verapamil is then continued after the cortisone is stopped. Constipation is common. Because of its efficacy and minimal side effects, verapamil is a mainstay of cluster prevention.

3. Lithium: Helpful for chronic cluster and, to a lesser degree, episodic cluster. Small doses, one to three of the 300 mg. tablets per day, are used for cluster headache. May be combined with verapamil and/or cortisone. Lithium is usually well tolerated in low doses; drowsiness, mood swings, nausea, tremor, and diarrhea may occur. Blood tests need to be done.

4. Indomethacin: This nsaid is helpful for some cluster patients; GI side effects may limit use.

Abortive Tension Headache Medications in Children (less than 11 years old)

1. Acetaminophen: Well tolerated, safe, not as effective as ibuprofen or aspirin. Chewable tablets and liquid are available. The usual dose is 5 to 10 mg/kg per dose. Because of safety, acetaminophen is the usual primary abortive medication to utilize in children. The addition of caffeine may enhance the effectiveness.

2. Ibuprofen: More effective than acetaminophen, but with occasional GI upset. Liquid Advil is available, which helps in younger children. Caffeine may enhance the effectiveness. The usual dose is 100 to 200 mg. Effective for migraine as well as tension headache.

3. Caffeine: Either used by itself, or with an analgesic, caffeine is useful for tension and migraine headache. In children, soft drinks containing caffeine are helpful. Side effects are minimal when caffeine is used in very limited amounts.

Abortive Migraine Medications in Children (less than 11 years old)

1. Ibuprofen, Acetaminophen, Caffeine: Ibuprofen is effective and available as a liquid, but GI upset is relatively common. Acetaminophen is very safe, less effective than the other abortives, but easy to use, with liquid and chewable forms available. For children who are nauseated and cannot swallow oral medication, compounding pharmacists are able to formulate acetaminophen into a lozenge, to be kept in the mouth and absorbed by the buccal mucosa. This may be combined, in a lozenge, with an antiemetic such as Phenergan or Tigan. Caffeine decreases migraine pain in most children, and may be used alone, or in combination with other abortives.

2. Naproxen (Naprosyn, Naprelan, Anaprox, Aleve): Naproxen is an effective abortive that is non-sedating and available as a liquid. GI side effects are very common, however. Adding small amounts of caffeine, such as in soft drinks, may enhance the effectiveness. Aleve (OTC) = 220 mg. naproxen.

3. Midrin: These are very large capsules that consist of a combination of a non addicting sedative, acetaminophen, and a vasoconstrictor. The capsules may be taken apart, and the Midrin swallowed with applesauce or juice. Sedation is common, as is lightheadedness. GI upset, although not very frequent, occurs at times. Brand name may be more effective than generic.

4. Butalbital medications (Fioricet, Esgic, Phrenilin): One-half tablet to 1 tablet every 6-8 hours as needed. Sedating. See “Butalbital (Fiorinal) Compounds”, and also First Line Migraine Abortive Medications.

Preventative Headache Medications in Children (less than 11 years old)

1. Cyproheptadine (Periactin): Cyproheptadine is a safe and generally effective first line headache preventive therapy. Fatigue and weight gain may be a problem, but it is usually well tolerated. Cyproheptadine is not as useful after age 11. It may be dosed once a day, and a convenient liquid form is available.

This guide is the author’s opinions; prescribing should be individualized, in conjunction with more complete medical references such as the PDR. Many of the listed medications do not have an FDA indication for headache. This guide is not prescriptive. This guide does not necessarily represent “standard consensus” treatment. This material may be copied.

2. NSAIDs (ibuprofen, naproxen): Ibuprofen and naproxen are available as a liquid, and the lack of sedation renders these very helpful for daily use. GI side effects are relatively common, and when these are used on a long-term basis, regular blood tests for hepatic and renal functions need to be done. Ibuprofen and naproxen may be utilized as daily preventives or as abortives for both tension and migraine headaches. Both are available OTC.

3. Propranolol (Inderal): Generally well tolerated, propranolol has been used for many years in children with migraine. Fatigue and decreased exercise tolerance may be a problem. With doses less than 60 mg. per day, we need to use propranolol twice per day, which is inconvenient for most children. Cyproheptadine or NSAIDs should usually be prescribed prior to propranolol.

4. Feverfew or Magnesium: See section on Natural Herbs/Supplements. Relatively safe, these carry less risk than the standard preventatives. Doses have not been established in children; I prescribe 1 feverfew capsule per day, or 80 mg. to 150 mg. magnesium oxide per day, depending upon weight.

Abortive Headache Medications in Adolescents (11 years and older)

1. At ages 11 and 12, the medications vary between those used for children and those for adults, depending upon weight and maturity. The NSAIDs (ibuprofen, naproxen), aspirin (with or without caffeine) and acetaminophen are most commonly utilized. Midrin is often used in adolescents. Triptans are being utilized with increasing frequency in adolescents. Many adolescents find the Imitrex nasal spray, or the Maxalt MLT (on the tongue) tablets useful at school. See earlier section on first line migraine abortive medications, plus Instructions for Patients on each triptan. The triptans are not yet FDA approved for adolescents, but there have been a number of positive studies.

Headache Preventative Medications in Adolescents

1. Antiinflammatories: Frequent GI upset is seen, but the NSAIDs usually do not cause fatigue or other cognitive effects. Ibuprofen (Motrin) and naproxen (Naprosyn, Aleve, Naprelan and Anaprox) are the NSAIDs most frequently utilized. Liquid preparations are available for both of these. Doses need to be kept to a minimum; hepatic and renal functions should be monitored via regular blood tests.

2. Depakote (Valproate): Useful for both migraine and CDH. Low doses (250 ER mg. once daily, or one Depakote ER 500 per day) are used. GI side effects, weight gain, or sedation may occur. Blood tests are done occasionally. See section on First Line Migraine Preventatives. The issue of polycystic ovarian syndrome in young women remains to be resolved.

3. Antidepressants: See Amitriptyline section, First Line Migraine Preventatives. Effective for migraine and daily headache. Nortriptyline (Pamelor), protriptyline (Vivactil), and amitriptyline (Elavil) are most commonly used. Usually well tolerated in low doses and safe for long term use. Cognitive side effects, dry mouth and dizziness are common. SSRI's and Effexor are useful, more for CDH than for migraine. The SSRI's are very helpful for comorbid anxiety and depression. See SSRI section. The small risk of suicidal thoughts, particularly in the 1st 30 days, must be understood by the patient and family. Risks/benefits need to be discussed.

4. Beta Blockers: See "First Line Preventative Medications for Migraine". Effective for migraine, and occasionally for daily headache. Propranolol (Inderal) and nadolol (Corgard) are most commonly utilized. Beta blockers may decrease exercise tolerance, which is a problem in this age range. Cognitive side effects also limit the utility of beta blockers. Low doses should be used.

5. Verapamil: See First Line Preventative Medications for Migraine. Effective for migraine, and occasionally, daily headache. Generally well tolerated, with constipation common. Convenient once per day dosing with the sustained release form. Low doses should be used in this age range.

6. Feverfew or Magnesium (see section on natural headache herbs): This safe herb has been proven to help prevent headaches; the usual dose is 1 or 2 capsules each morning. Magnesium oxide is also safe and well tolerated.

SSRI's (Selective Serotonin Reuptake Inhibitors)

Chronic anxiety is a problem in approximately 60% of migraine patients. Dysthymia or major depression are seen in 15% of migraineurs. Migraineurs are 12 times more likely to have panic disorder than those without migraine. The chronic anxiety or depression leads to a decreased quality of life in migraine patients. These comorbidities of anxiety or depression are a physical, genetic problem, just like migraines. The selective serotonin reuptake inhibitors (SSRI's) have been very effective in combating anxiety and depression. They also are somewhat helpful in preventing migraine or tension headache. Large-scale studies have not revealed SSRI's to be more than mildly helpful for preventing headaches. However, they continue to be widely used throughout the United States for headache patients because of the positive effect on anxiety and depression. The low incidence of adverse reactions is another factor in the widespread use of SSRI's.

The safety and efficacy of the major SSRI's (Prozac/Zoloft/Paxil/Celexa/Lexapro) in treating anxiety or depression is well established. Although SSRI's are not as effective as tricyclics (amitriptyline, nortriptyline, etc.) for pain, they have a very favorable side effect profile. The SSRI's have less of the dry mouth, constipation, weight gain and sedation seen with the tricyclics. SSRI's are also a safer choice in the elderly, primarily due to tolerability, and the lack of cardiac side effects.

Side Effects

The major SSRI's do differ somewhat in their side effect profile. Some patients do extremely well with one SSRI, but not with another. The most common side effects are: nausea, drowsiness or fatigue, dry mouth, anxiety, insomnia, decreased libido, impotence, asthenia, sweating, constipation, tremor, diarrhea and anorexia. Weight gain may be a major problem. Many of the side effects are dose related. Minimizing the dose can, for instance, decrease the sedation or sexual side effects. One key to minimizing side effects is to begin with low doses. Compliance is enhanced when the SSRI's are slowly titrated. The initial anxiety seen with SSRI's often abates if low enough doses are utilized. Since any antidepressant can trigger hypomania or mania in bipolar patients, it is prudent to "start low and go slow". Weight gain and sexual side effects are the most common reasons for discontinuation.

Seven Keys To Using SSRI's in Headache Patients

1. Start with very low doses. This minimizes sedation and anxiety and increases compliance.
2. If patients are warned about the initial anxiety that may occur with SSRI's, they are more likely to be compliant and stay on the medication.
3. For most headache patients, lower doses are utilized than for severe depression.
4. If one SSRI does not help or causes side effects, it is very often worthwhile to try another. Patients have widely differing responses to these medications.
5. Slowly withdraw patients in order to avoid the withdrawal syndrome.
6. If the headaches are exacerbated, discontinue the SSRI.
7. Paroxetine (Paxil), fluoxetine (Prozac), and duloxetine (Cymbalta) have more drug interactions than the others.

The Major SSRI's

Fluoxetine (Prozac): Prozac is available in 10 mg., 20 mg., 40 mg. pulvules; 10 mg. scored tablets; liquid=20 mg./5 ml. Prozac Weekly is a once a week capsule, equal to 20 mg. daily. A generic form of Prozac is now available. Prozac is the prototype SSRI, having been used in over 50 million patients in the United States. Prozac is a long-acting (elimination half-life=4 to 6 days, but the active metabolite, norfluoxetine, has an elimination half-life of 4 to 16 days) SSRI with a well-established track record. The long half-life is generally an advantage in avoiding the SSRI withdrawal syndrome. It is important to start with low doses of SSRI's; 5 or 10 mg. of Prozac is a good starting point. Many patients report initial anxiety (or even panic) from SSRI's, and if they are on a low enough dose, they are less likely to discontinue the medication. Patients can begin with ½ tablet of 10 mg. Prozac.

Over 4 to 10 days, the dose may be raised to 10 or 20 mg. The effective dose for migraine or tension headache varies widely, from 5 mg. per day to 60 mg. (or more). Most patients are on 20 mg. daily. Milder tension-type headache often responds to low doses (10 or 20 mg). As is true with tricyclics, lower doses of SSRI's are used for headache than for major depression. In some patients, SSRI's actually exacerbate headaches. It is too early to determine if the generic fluoxetine is as effective as the brand (Prozac). Fluoxetine is an inhibitor of the 2D6 system, and to a lesser extent 3A4 as well.

Sertraline (Zoloft): Zoloft is available in 25 mg., 50 mg. and 100 mg. scored tablets. Zoloft is somewhat shorter-acting; elimination half-life=26 hours of the parent drug and 62 to 104 hours of the active metabolite. Because the half-life is shorter than with Prozac, patients are occasionally able to stop Zoloft for one or two days and alleviate the sexual side effects. However, with the shorter half-life, withdrawal syndrome is occasionally seen with Zoloft. I usually start with 25 mg., or ½ of a 25 mg. tablet, and slowly increase; the average antidepressant dose is 75 to 150 mg., but the usual headache dose is approximately 50 mg. While many patients are on 100 mg. or more for headaches, most patients are maintained on lower doses. The cost of the 50 mg. and 100 mg. tablets is approximately the same. In higher doses, Zoloft is a 2D6 and 3A4 inhibitor.

Paroxetine (Paxil): Generic is available. Paxil is conveniently available in 10, 20, 30 and 40 mg. tablets. Paxil CR (controlled release) is available in 12.5 and 25 mg. doses. The elimination half-life is 21 hours, with no active metabolite. Paxil is generally very well tolerated. I usually begin with ½ of a 10 mg. tablet and slowly increase to 10 or 20 mg.; many patients need 30 to 60 mg. for depression. Or, we start with 12.5 mg. CR and titrate as needed to 25 mg. CR. It is important to stop Paxil slowly in order to minimize withdrawal. Paxil (SSRI) withdrawal consists of one to several days (and occasionally longer) of flu-like symptoms, malaise, dizziness and asthenia. This often goes unreported to the physician. Managing the withdrawal can be difficult; at times, the addition of fluoxetine (Prozac) may help in weaning off of the short-acting SSRI. Paroxetine is a potent inhibitor of the 2D6 system and, to a lesser extent, 3A4. See section on cyp enzymes.

Citalopram (Celexa): Celexa is available in 20 and 40 mg. tablets, which are scored. The mean terminal half-life is about 35 hours. Celexa has a clean profile with regard to cytochrome P450 enzymes. Celexa has been an outstanding antidepressant with a very good track record, and is well tolerated. Side effects are similar to the other SSRI's. As always, we start with low doses, half of a 20 mg. tablet for four to six days, then progress to 20 mg. per day. Withdrawal symptoms have been unusual with Celexa. Its use has mostly given way to Lexapro.

Escitalopram (Lexapro): Lexapro is available in 10 and 20 mg. tablets. Lexapro is metabolized primarily by the liver. Lexapro is a newer, more selective version of Celexa and has been fairly well tolerated. Lexapro has a favorable side effect profile, but side effects are similar to the other SSRI's. We start with ½ of the 10 mg. tablet for 4 to 6 days, and then increase to 10 mg. daily. Withdrawal symptoms are relatively unusual with Lexapro. It is fairly clean as far as drug interactions.

Wellbutrin, Remeron, Effexor, and Cymbalta

Wellbutrin (bupropion): Wellbutrin is actually an older antidepressant that is in its own class (aminoketone). It is unlike tricyclics or SSRI's. Wellbutrin is available in lower doses. A generic SR is available; the XL form is once daily, 150 mg. or 300 mg. The usual dose is 100 or 150 mg. slow release tablets once per day. For moderate to severe depression, the doses are pushed to 300 mg. or more per day. Wellbutrin (bupropion) may work primarily through norepinephrine pathways. The advantages of Wellbutrin are that sedation, weight gain and sexual side effects are much lower than many of the other antidepressants. In fact, weight gain has been no more than placebo and the sexual side effects are exceedingly low. At higher doses, particularly at 300 mg. per day or more, people who are predisposed to seizures are at a slightly increased risk for seizure. This is dose related and is approximately .1 % (1 out of 1,000) at 300 mg. per day, increasing to .4% at 400 mg. per day. In treating headache patients, we usually use lower doses.

Wellbutrin is also utilized for smoking cessation (under the name Zyban). While it is not as anxiolytic as SSRI's, the lack of sexual side effects and weight gain render this an excellent antidepressant. The efficacy for depression is somewhat less than with the SSRI's and Effexor.

Remeron (mirtazipine): Remeron is available in 15 mg., 30 mg., and 45 mg. film coated tablets, and is also available in dissolving tablets. Generic is available. Remeron enhances noradrenergic and serotonergic activity. Remeron is also an antagonist of histamine, which helps to explain its sedative effects. The usual dose is 30 mg. per day; however, we start with 7.5 or 15 mg. at night for a period of time before increasing to 30 mg. Somnolence is very common, but this is an advantage in agitated depressed patients with insomnia. Weight gain is commonly seen, and is a major limiting side effect. Overall, Remeron has fewer side effects than the older tricyclics. While its primary use is in depression, for which it is a very effective medication, headache is sometimes improved with Remeron. Remeron is commonly used as an adjunctive medication for severe, refractory depression.

Effexor (venlafaxine): Effexor is available in 25 mg., 37.5 mg., 50 mg., 75 mg. and 100 mg. tablets. The long-acting Effexor XR is available in 37.5 mg., 75 mg. and 150 mg. doses. Effexor has been an outstanding antidepressant because of efficacy and tolerability. Effexor is basically an SSRI in low doses; at higher doses, norepinephrine, then dopamine, are affected. It is very well tolerated, with less weight gain and sexual side effects than some of the other antidepressants. Effexor has few interactions with cytochrome P450 enzymes, rendering it a fairly clean medication. We usually begin with 37.5 mg. and progress to 75 mg., with a typical dose in headache patients being 75 mg. or 150 mg. Effexor XR is particularly well tolerated. Studies on Effexor for headache are pending, but it is very useful in headache patients who have concurrent anxiety and depression. Sustained elevation in blood pressure may occur at higher doses, particularly 250 mg. per day or more. The lower doses have not increased blood pressure. While headache is a potential side effect of Effexor (and all of the others), it has been no more than the rate of placebo in studies. Nausea, constipation, somnolence, dry mouth, dizziness, insomnia and agitation are seen more than in placebo. However, if doses remain low, Effexor has been well tolerated. While Effexor is less effective than tricyclic antidepressants for pain or headache, its efficacy in anxiety and depression, and its tolerability render it an extremely useful medication.

Cymbalta (duloxetine): Cymbalta increases both serotonin and norepinephrine. It is available in 20, 30, and 60 mg. capsules (which should <u>not</u> be split apart). Early reports indicate that Cymbalta may be helpful for headache, as well as for anxiety/depression. 60 mg. daily is the usual dose for depression; the starting dose is 20 or 30 mg., increasing over days to weeks. Side effects include, among others, nausea, dry mouth, anxiety, fatigue, lethargy, sexual effects, and weight gain. Use with caution in patients with glaucoma. Cymbalta is a moderate CYP 2D-6 inhibitor. See CYP enzyme system section.

Treatment of Insomnia in Headache Patients

Insomnia is commonly seen in migraine and chronic daily headache patients. The following are Rules for Better Sleep:

Sleep as much as needed to feel refreshed and healthy during the following day, but not more. Curtailing the time in bed seems to solidify sleep; excessively long times in bed seem related to fragmented and shallow sleep.

A regular awakening time in the morning strengthens circadian cycling and, finally, leads to regular times of sleep onset.

A steady daily amount of exercise probably deepens sleep; occasional exercise does not necessarily improve sleep the following night. Yoga may be helpful. Deep breathing / relaxation exercises may help.

Occasional loud noises (e.g. aircraft flyovers) disturb sleep even in people who are not awakened by noises and cannot remember them in the morning. Sound attenuated bedrooms may help those who must sleep close to noise. White noise sound machines (such as at Brookstone) help to blunt outside sounds. Consider ear plugs (Hearos, 33db, is a particularly good brand). These are also helpful on a plane, or on vacation.

Although excessively warm rooms disturb sleep, there is no evidence that an excessively cold room solidifies sleep.

Hunger may disturb sleep; a light snack may help sleep.

An occasional sleeping pill may be of some benefit, but their chronic use is ineffective in most insomniacs. However, some people do well on sleeping pills for months or years.

Caffeine in the evening disturbs sleep, even in those who feel it does not.

Alcohol helps tense people fall asleep more easily, but the ensuing sleep is then fragmented.

People who feel angry and frustrated because they cannot sleep should not try harder and harder to fall asleep, but should turn on the light and do something different.

The chronic use of tobacco disturbs sleep.

Go to bed only when sleepy.

Keep a night light in the bathroom (bright lights will awaken your brain).

Use the bed only for sleeping; do not read, watch television or eat in bed.

If unable to sleep, get up and move to another room. Stay up until you are really sleepy, then return to bed. If sleep still does not come easily, get out of bed again. The goal is to associate bed with falling asleep quickly. Repeat this step as often as necessary throughout the night.

Set the alarm and get up at the same time every morning, regardless of how much you slept during the night. This helps the body acquire a constant sleep/wake rhythm.

Do not nap during the day.

While medications are often ineffective for chronic insomniacs, at times they may be helpful. The sedating antidepressants (amitriptyline, other sedating tricyclics, trazodone, Remeron, etc.) may be helpful both in helping sleep and headaches the next day. While benzodiazepines may be helpful, they are somewhat of a last resort to be utilized on a long-term basis. The two primary sleeping aids that are used are zolpidem (Ambien) and zaleplon (Sonata). Ambien is somewhat longer acting that Sonata. The usual dose is ½ or 1 10 mg. tablet qhs. Side effects tend to be minimal, but the patient may be sedated in the morning. Occasionally other cognitive problems will occur the next morning. Sonata is shorter acting, and may be dosed for middle-of-the-night insomnia. The usual dose is 5 or 10 mg., either qhs, prn, or in the middle of the night prn. Ambien and Sonata are both very safe, but both are potentially habit forming. Newer ones will be available soon.

In addition to the above, the atypical antipsychotics are occasionally utilized in selected patients. These are particularly helpful in those patients with bipolar illness, or very severe anxiety. The usual medication would be Seroquel 25 mg. ½ or 1, or 2, qhs, or Zyprexa 2.5 mg. or 5 mg. qhs. Fatigue may occur with both of these the next day, and waking is seen relatively often with Zyprexa. These atypicals do have the possibility for long term side effects (tardive dyskinesia, diabetes), and therefore are used only in selected patients where the benefit may outweigh the risk.

Certain muscle relaxants may aid sleeping. Zanaflex, (tizanidine) 4 mg., ½ or 1, is not addicting, and may be helpful in preventing the headaches the next day. Cyclobenzaprine (Flexeril) is also sedating, not addicting, and helpful for those with neck or back pain.

Benzodiazepines are not the first-line meds, but do play a role in selected patients. The chronic use of benzodiazepines may actually increase pain or headache the next day.

Bipolar Illness and Migraine

The comorbidity of migraine with anxiety and depression is well established, both in clinically based studies and in epidemiologic samples from community populations. The physiologic overlap between migraine and depression is considerable, and antidepressants or mood stabilizers often help both conditions. In the vast majority of migraine patients who suffer from depression, anxiety is a complicating factor. The anxiety disorder often precedes the age of onset of migraine, with depression following afterward.

It is possible that poorly controlled migraine headaches may fuel the onset of depression or depression may, at times, increase headache. However, it is more likely that shared environmental and genetic factors link migraine and depression.

The relationship between bipolar illness and migraine has not been as well studied as depression and migraine. However, in several studies bipolar I and bipolar II were found to be increased in migraineurs. In our study, ("The Bipolar Spectrum in Migraine Patients", Robbins, L., Ludmer C., *American Journal of Pain Management*, October, 2000, Vol. 10, No. 4, pp. 167-170) we assessed 1000 consecutive migraineurs. The results were as follows: Bipolar I: 2.1 %; Bipolar II: 2.4%; Cyclothymic Disorder: 1.3%; Bipolar Disorder Not Otherwise Specified: 2.8%; Total Bipolar Spectrum: 8.6%.

The clinical spectrum of bipolar disorders is an evolving concept. The DSM has historically inherent biases against independently diagnosing bipolarity, and bipolar II is defined very conservatively in DSM-IV. For example, in DSM-IV, the important hypomanic reaction to an antidepressant is not included in helping to determine bipolarity. Some authors feel DSM-IV has an inherent bias towards diagnosing personality disorders, rather than bipolar disorders. These biases lead to bipolar disorders being missed and underdiagnosed.

It is the milder end of the bipolar spectrum that tends to be missed; those with persistently agitated, angry personalities, with frequent depressions and/or "too much energy", with a strong bipolar family history, may not have a clear hypomanic or manic episode.

The therapeutic implications for recognizing bipolarity are enormous. These patients, when not diagnosed, often are given a number of antidepressants, with

predictable hypomanic results. The tricyclic antidepressants appear to have the highest propensity towards triggering mania, followed by the selective serotonin reuptake inhibitors (SSRI's).

Once the bipolar diagnosis is established or suspected, mood stabilizers often are very helpful for the moods and headaches. Divalproex sodium (Depakote) is effective for mania, hypomania, depression associated with bipolar disorder, and for headache prevention. Divalproex sodium has been extremely well studied for these conditions, and has become one of the primary migraine and chronic daily headache preventives. Lithium carbonate is not utilized as readily in the headache population, due to increased side effects, as well as lack of efficacy for migraine. One or more of the newer antiepileptics may prove to be helpful for bipolar disorders and/or migraine. Carbamazepine (Tegretol) has some utility as a mood stabilizer, but not for migraine prophylaxis.

Topamax may improve moods in some patients. Trileptal may prove to be one of the better mood stabilizers.

Lamictal is becoming one of the most commonly used mood stabilizers. It is one of the only effective medications for bipolar depression. Doses must be slowly titrated, due to the 1 or 2 out of 1000 severe allergic reaction. Lamictal may increase headache, but is usually well tolerated.

The Atypicals (see next section) are also used for bipolar. When a mood stabilizer is effective, the underlying agitation/anger/depression improves.

The recognition of an increased comorbidity between migraine and bipolar illness has important clinical implications. By broadening our concept of the bipolar realm, we can improve outcome in these patients.

The Use of “Atypicals” in the Headache Patient

The newer “atypical” antipsychotics have been useful in several situations for selected headache patients. For a patient with a moderate or severe personality disorder, the atypicals may ease the anxiety and/or depression. They can be an effective mood stabilizer in bipolar. They also are helpful for insomnia. These medications may be useful as a headache abortive, primarily because of the induction of sedation and sleep. One commonly used atypical is quetiapine (Seroquel), 25-100 mg. qhs. It is very important to attempt to use as low a dose as possible. The doses for headache patients with severe anxiety or insomnia tend to be lower than the standard doses of these for schizophrenia. Seroquel is usually well tolerated, with sedation being the primary side effect the next day. Because of the risk of long-term side effects, particularly tardive dyskinesia, and diabetes, these should only be used in the occasional selected patient where benefit outweighs risk. Patients must be aware of the possible side effects, such as weight gain. Olanzapine (Zyprexa) has also been utilized in a similar fashion. The usual dose is 2.5 or 5 mg. qhs. Occasionally, Seroquel or Zyprexa have been used on a prn basis with headache patients. These help induce sleep, and may offset nausea as well. The other atypicals may also be useful. Ziprasidone (Geodon) and aripiprazole (Abilify) are also available, with much less tendency toward weight gain. While sedation is the most common side effect to all of these atypicals, the following are also seen relatively often: nausea, dizziness, restlessness, tremor, rash, diarrhea, or constipation. Hypomania may occur. While QT prolongation may occur with any of the antipsychotics, this may possibly be more of a concern with higher doses of Geodon. The potential for some of these newer “Atypicals” to possibly cause an increase in blood sugar is a serious concern that may limit these medications in certain patients.

Fatigue

Fatigue is a symptom commonly reported by headache patients. Two studies have indicated that 50% of migraine patients report significant “excessive daytime sleepiness”. Unfortunately, little is understood about its cause. The following medications are sometimes utilized to treat fatigue:

1. **Provigil** (modafinil): This fairly safe medication is classified as a wake-promoting agent. Usual doses start at 100 mg. daily and occasionally are increased up to 400 mg. a day if needed. Most patients are on 200 mg. a day. The most common side effects with this medication are headache, nausea and anxiety. Unfortunately, Provigil may actually increase headache.

2. **Stimulants** (dextroamphetamine, methylphenidate, Adderall): These medications may be helpful for fatigue, as well as concurrent ADD/ADHD. They may help to decrease pain or headache as well. Some of these medications come in short-acting and long-acting preparations, which is helpful. The main side effects consist of decreased appetite, insomnia and dry mouth.

3. **Wellbutrin** (bupropion): This medication is an antidepressant which is beneficial due to its activating nature. The doses are available in SR slow-release tablets 100 mg., 150 mg., and 200 mg. tablets, along with a once-daily XL form, which comes in 150 mg. and 300 mg. dosage. Depending on comorbid anxiety and depression, the dose range may vary from 100 mg. up to 300 mg. per day. The advantages of Wellbutrin are that sedation, weight gain and sexual side effects are much lower than with many of the other antidepressants. See previous section on Wellbutrin.

The CYP 450 Enzyme System

We have tried to be accurate, but different reference sources vary as to these systems.

Drug-Drug interactions are important to understand prior to starting a new medication. All medications go through various routes of elimination. A subset of enzymes found in the liver, known as CYP isoenzymes, are responsible for metabolism of many common medications. Some medications are substrates for one of these enzymes, in many cases meaning that they are converted into a less active form than the parent compound. Various medications may act as inducers or inhibitors of these enzymes. The inducers “speed up” the action of these enzymes. The inhibitors “slow down” the action of these enzymes. Thus, inducers may decrease the effectiveness of particular drugs that are substrates for the same isoenzyme while inhibitors have the opposite effect.

The most common isoenzymes that have relevance to our practice are: CYP 2D6, CYP 3A4, CYP 1A2, CYP 2C9, CYP 2C19, and CYP 2B6.
The lists below are not complete. Prior to starting a new medication not listed below, one should consult the PDR for interactions.

CYP2D6

Bold = strong effect

Substrates	**Inhibitors**	**Inducers**
Amitriptyline	**Chlorpromazine**	**None**
Aripiprazole (and 3A4)	Clomipramine	
Atomoxetine	Desipramine	
Captopril	Diphenhydramine	
Chlorpromazine	**Duloxetine (Cymbalta)**	
Clomipramine (and 1A2, 2C19)	**Fluoxetine**	
Codeine	Imipramine	
Desipramine	Ketoconazole	
Dextroamphetamine	Methadone	
Doxepin (and 1A2, 3A4)	**Paxil** (Paroxetine)	
Duloxetine	Sertraline (if > 150 mg.)	
Fluoxetine (and 2C9)	Trazodone	
Hydrocodone	**Miconazole**	
Imipramine (and 2C19)		
Labetalol		
Methylphenidate		
Metoprolol		

2D6 Substrates, continued

Mirtazapine (and lA2, 3A4)
Nortriptyline
Oxycodone
(converted to active metabolite-inhibitors
decrease overall efficacy)
Paroxetine
Pindolol
Promethazine (and 2B6)
Propanolol (and 2C19, lA2)
Protriptyline
Risperidone
Timolol
Tramadol
Venlafaxine (and 3A4)

Interestingly, 14% of patients are “poor metabolizers”. The CYP 2D6 enzyme doesn’t work as efficiently, in those patients
Also, tramadol, hydrocodone, and oxycodone are metabolized to various forms.
Oxycodone-➔ oxymorphone (15% of parent, weaker met), inhibitors to CYP 2D6 have unknown significance
Oxycodone-➔ noroxycodone (majority of parent) not inhibited by CYP2D6
Tramadol-➔ Ml metabolite (active form of drug), inhibitors may decrease analgesic effects
Hydrocodone-➔ hydromorphone (active form of drug), same as tramadol: inhibitors may decrease effect.

CYP 3A4

Substrates	**Inhibitors**	**Inducers**
Alprazolam	Caffeine	
Aripiprazole (and 2D6)	Cimetidine	**Tegretol**
Atorvastatin	**Ciprofloxacin**	**Phenytoin**
Buprenorphin	**Clarithromycin**	**Trileptal**
	Desipramine	**(?>1200)**
Buspirone		
	Diltiazem	**Phenobarbital**
Cerivastatin		
Chlordiazepoxide	**Doxycycline**	
Clarithromycin	Erythromycin	
	Fluconazole	

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CYP 3A4, continued

Substrates	**Inhibitors**
Clonazepam	Grapefruit Juice
Diazepam (and 2C19)	**Itraconazole**
Dihydroergotamine	**Ketoconazole**
Diltiazem	**Antiretrovirals**
Doxepin (and lA2, 2D6)	Metronidazole
Eletriptan	**Miconazole**
Erythromycin	Nefazodone
Escitalopram (and 2C19)	Norfloxacin
Estrogens (and lA2)	Sertraline
Fentanyl	Tetracycline
Lansoprazole (and 2C 19)	Verapamil
Losartan (and 2C9)	
Lovastatin	
Methadone	
Mirtazapine (and lA2, 2D6)	
Modafinil	
Montelukast (and 2C9)	
Nifedipine	
Ondansetron	
Quetiapine	
Setraline (and 2B6, 2C9, 2C19)	
Sildenafil	
Simvastatin	
Tiagabine	
Trazodone	
Triazolam	
Venlafaxine (and 2D6)	
Verapamil	
Zaleplon	
Zolpidem (partial)	
Zonisamide	

*Pravastatin has multiple pathways...may want to use if pt is on CYP 3A4 inhibitor

<u>CYP 1A2</u>

Substrate	**Inhibitor**	**Inducer**
Cyclobenzaprine	**Caffeine**	**Phenytoin/PB**
Doxepin (and 2D6, 3A4)	**Ciprofloxacin**	**Tegretol**
Frova	Diclofenac	*Brocoli*
Zomig	Prozac	*Caffeine*
Olanzipine		*Smoking*
Clomipramine (and 2C19, 2D6)		

CYP 1A 2, *continued*

Substrates	**Inhibitors**
Estrogen	Gemfibrozil
Mirtazapine (and 2D6, 3A4)	**Ketoconazole**
Propanolol (and 2C19, 2D6)	**Norfloxacin**
	Nifedipine
	Rofecoxib
	Miconazole

CYP2C9

Substrate	**Inhibitor**	**Inducer**
Fluoxetine (and 2D6)	Provigil	**Tegretol**
Losartan	**Fluconazole**	**Phenobarb**
Montelukast (and 3A4)	**Flurbiprofen**	**Phenytoin**
Sertraline (and 3A4, 2B6,2C19)	Fluvastatin	
Warfarin	**Gemfibrizol**	
NSAIDS	**Ibuprofen**	
	Indocin	
	Ketoconazole	
	Miconazole	
	Losartan	
	Omeprazole	
	Pantoprazole	
	Sulfamethoxazole	
	Zafirlukast	

CYP 2C19

Substrate	**Inhibitor**	**Inducer**
Amitriptyline	**Fluconazole**	**Tegretol**
Clomipramine (and lA2, 2D6)	Fluoxetine	**Phenytoin**
Diazepam (and 3A4)	**Gemfibrozil**	
Escitalopram (and 3A4)	Ketoconazole	
Esomeprazole	Lansoprazole	
Lansoprazole (and 3A4)	Loratadine	
Sertraline (and 3A4, 2B6, 2C9)	Modafinil	
	Omeprazole	
	Miconazole	

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CYP 2C19, *continued*

Substrates	**Inhibitors**
Imipramine (and 2D6)	Rabeprazole
Omeprazole**	Sertraline
Pantoprazole	
Progesterone	
Propanolol (and lA2, 2D6)	

** Try Prevacid, Axid, Aciphex, Pepcid or Protonix instead

CYP 2B6

Substrate	**Inhibitors**	**Inducers**
Wellbutrin	Desipramine	Orphenadrine
Promethazine	Paroxetine	**Tegretol**
	Sertraline	**Phenytoin**
		Phenobarbital

Instructions For Patients: Maxalt (Rizatriptan)

Maxalt is a well-tolerated, effective triptan. Maxalt is available in 5 mg. and 10 mg. strengths. Maxalt MLT are tablets that dissolve in seconds on the tongue. In general, the side effects have been found to be minimal. Side effects are very similar to those of Imitrex. These include nausea, chest heaviness or pressure, pressure in the throat, shortness of breath, rash, tingling sensation, heat sensation or heaviness, tiredness, drowsiness, dizziness, etc. The symptoms are usually short-lasting. They go away, but, if they are more than mild, Maxalt should not be taken again until you speak with the physician. We are careful with Maxalt (and all triptans) in patients who have major risk factors for heart problems. Maxalt should not be used in people with hardening of the arteries or who have had past heart attacks. However, in all of the studies and previous experience with Maxalt, it has generally been a safe medication.

How To Use Maxalt Tablets

The earlier one uses Maxalt for a migraine, the better. Maxalt, 10 mg., may be taken one every three to four hours, as needed, three in a day at most. Most patients have only needed one tablet. The tablets are generally limited to 10 tablets per week at most. The very first time you use it, try ½ tablet only to see how you will react. Maxalt MLT tablets should be put on the tongue (they dissolve in seconds). Patients usually like the MLT tablets because of convenience; these do not require water.

Maxalt With Other Medication

Maxalt should not be taken in the same day as other ergotamines (such as Cafergot) and should not be taken in the same day as Imitrex, Amerge, Axert, or Zomig. Pain medications (such as aspirin, Aleve, ibuprofen, Fiorinal, Vicodin, Tylenol, etc.) may be used, even at the same time. In some patients, this increases efficacy. Anti-nausea medications may also be used at the same time. Generally, there are relatively few interactions between Maxalt and other medications.

How Long Does It Take To Work?

Maxalt can take anywhere from 20 minutes to two hours to help.

Instructions for Patients: Relpax (Eletriptan)

The earlier in a migraine, the better Relpax works. Relpax is an effective and well-tolerated triptan. It is available in 20 and 40 mg. strengths. The side effects have, in general, been found to be fairly minimal. They are similar to Imitrex's. These include possible nausea, pressure in the throat, dizziness, and tiredness or weakness. Although chest pressure/pain/tightness may occur with Relpax, these symptoms have not been seen very often (only 1 to 2% of patients). In long-term studies, only 8.3% of patients discontinued the Relpax due to side effects.

Who Should Not Use Relpax

As with any other triptan, the following conditions should mitigate against the use of Relpax: 1. hypertension that is not well controlled, 2. past history of a stroke, 3. history of heart disease, 4. circulatory problems, 5. basilar or hemiplegic migraine, and 6. Relpax should not be used with nefazodone (Serzone), Nizoral, Sporonox, verapamil, TAO, Biaxin, Norvir and Viracept. These medicines may increase the concentration of Relpax; a few other medications are contraindicated, please check the PI for the list. Any triptan can cause a short-term increase in blood pressure. Serious cardiac events have occurred following the use of triptans.

How To Use Relpax

The tablets are available in 20 and 40mg. The usual dose is 40 mg, which may be repeated in 2 to 4 hours, if needed. 80 mg. per day (2 of the 40 mg tablets) is the recommended maximum. The very first time that patients use a triptan such as Relpax, I usually recommend that they take ½ tablet only, then repeat the other half in 30 to 45 minutes. After the initial time, we usually utilize the whole tablet.

Relpax With Other Medication

Relpax should not be used in the same day as ergotamines (Migranal) or other triptans (Imitrex, Zomig, Maxalt, Axert , Frova). Nefazodone (Serzone) and a few other CYP3A4 inhibitors are contraindicated with Relpax.

Pain medications (such as aspirin, Aleve, ibuprofen, Fiorinal, Vicodin, Tylenol, etc.) may be used even at the same time as Relpax. Combining these with Relpax will, at times, increase efficacy. Anti-nausea medications may also be used at the same time.

How Long Does Relpax Take To Work?

Relpax may take from 30 minutes to 2 hours to become effective. After a 40 mg. dose, 55% to 65% of patients have mild or no headache after 2 hours.

Instructions For Patients: Zomig Tablets and Nasal Spray (N.S.)

Zomig N.S. is a fast-acting triptan. It is very effective, and may work as soon as 15 to 25 minutes. SE's are similar to the tabs; a mildly unpleasant taste may occur. Zomig tabs are very similar to Imitrex tablets. It is available in 2.5 mg and 5 mg. tablets. The Zomig ZMT (on the tongue) is 2.5 mg or 5 mg. The side effects have, in general, been found to be minimal. Side effects are very similar to those of Imitrex. These include chest heaviness or pressure, pressure in the throat, nausea, shortness of breath, rash, swelling of the face or lips, tingling, heat or a sensation of heaviness, tiredness, drowsiness, dizziness, etc. Most of these symptoms are not seen with Zomig, or, if they occur, they are short lasting. They go away and, if they are more than mild, the Zomig should not be taken again until you talk with your physician. We are careful with Zomig or Imitrex in patients who have major risk factors for heart problems. Zomig should not be used in people with hardening of the arteries or who have had past heart attacks. However, in all of the studies and previous experience with Zomig, it has generally been a safe medication. The earlier Zomig is used for a migraine, the better.

How To Use Zomig Tablets and Nasal Spray

Zomig 5 mg. tablet or the 5 mg. ZMT (dissolvable tablet on the tongue) may be taken every three to four hours as needed. Many patients need 5 mg. at a time, every three to four hours, as needed, with 10 mg. per 24 hours at most (or two of the 5 mg. tablets per 24 hours at most). The tablets are limited to 10 tablets per week at most. The ZMT (dissolvable) has a pleasant orange taste. The Zomig N.S. is dosed at 1 spray every 3 hours, as needed, 2 sprays (10mg) in a day at most.

Zomig With Other Medication

Zomig should not be taken in the same day as Imitrex or other triptans. Pain medications, such as aspirin, naproxen, ibuprofen, Fiorinal, Vicodin, Tylenol, etc, may be used, even at the same time as Zomig. Anti-nausea medication may be used at the same time. Generally, there are relatively few interactions with Zomig.

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Instructions For Patients: Axert

Axert is a well tolerated triptan, available in 6.25 mg. and 12.5 mg. tablets. The side effects are generally mild, and include: possible nausea, pressure in chest or throat, shortness of breath, tingling sensation, fatigue, dizziness, etc. The side effects, if experienced, usually resolve within ½ hour. If you have more than mild side effects, do not take Axert again until you speak with your physician. As with other triptans, people with major risk factors for coronary artery disease should be screened prior to using Axert. Axert has generally been a safe medication.

How To Use Axert

Axert, 12.5 mg., may be taken every 2 hours, as needed, 2 in a day at most. The tablets are usually limited to 10 per week at most. The very first time you use it, try ½ tablet to see how you will react. Axert usually takes ½ hour to 1 hour to help. The earlier one uses Axert for a migraine, the better.

Axert With Other Medications

Axert should not be taken in the same day as triptans (Imitrex, Amerge, Maxalt, Zomig). Pain medications and OTC's (such as aspirin, ibuprofen, Aleve, Fiorinal, Vicodin, etc.) are OK to use with Axert, even at the same time. Sometimes using ibuprofen or naproxen (Aleve) with a triptan such as Axert increases the effectiveness. Anti-nausea medications may be used at the same time. Axert has relatively few medication interactions.

Instructions For Patients: Frova (Frovatriptan)

Frova is usually 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. Side effects are similar to those of Imitrex.

Who Should Use Frova?

Frova is most useful for migraines that are of slower onset; if one awakens with a very severe migraine with severe nausea, Frova may not be the optimal choice. It is common for migraineurs to experience prolonged moderate or moderate to severe migraines. Menstrual migraines are often of long duration. Frova, with its extended duration of action, is an ideal triptan for these patients. As with any migraine abortive, early intervention with the medication is best.

Who Should Not Use Frova?

As with other triptans, the following conditions should mitigate against the use of Frova: 1. hypertension that is not well controlled; 2. past history of a stroke; 3. history of heart disease; 4. circulatory problems; and 5. basilar or hemiplegic migraine. Any triptan can cause a transient increase in blood pressure.

How to use Frova Tablets

Frova is available in 2.5 mg tablets. Frova tablets are less expensive than most of the other available triptans. The usual dose is 2.5 mg every 2 to 4 hours as needed, 3 tablets in 24 hours at most.

Frova With Other Medications

As with other triptans, Frova may be used in conjunction with most other medications such as nsaids or analgesics. At times, I do sometimes suggest to patients that they combine an nsaid (such as naproxen) with a triptan, in an attempt to prevent headache recurrence. Antiemetics are safe with Frova.

Frova should not be used in the same day as other triptans (Imitrex, Amerge, Axert, Zomig, Maxalt). If an ergotamine has been ingested in the previous 24 hours, Frova should not be utilized.

Side Effects

Frova has been exceptionally well tolerated. As with other triptans, certain patients will experience 20 to 30 minutes of mild side effects. These include dizziness, paresthesias, flushing and fatigue. In addition, feelings of hot or cold, dyspepsia, skeletal pains, dry mouth, or (brief) headache may occur. All triptans may provoke chest pain, which is rarely of cardiac origin.

The serious side effects of triptans, as a class, include myocardial infarction and stroke. Over 50 million patients have taken triptans, and serious adverse events are extremely rare. Prior to triptan use, patients should be screened for risk factors associated with coronary artery disease or spasm. If moderate to severe chest pain does occur after the use of any triptan, it is prudent to discontinue use, at least until appropriate cardiac evaluation is accomplished.

Frova With Pregnancy or Nursing

Frova should not be used during pregnancy (it is category C). Frova should not be used by a woman who is nursing.

Instructions For Patients: Amerge (Naratriptan)

Amerge is a smooth, long-acting triptan, extremely well tolerated. It is available in 1 mg. and 2.5 mg. strengths. In general, the side effects have been found to be minimal. These include possible nausea, chest heaviness or pressure, pressure in the throat, shortness of breath, rash, tingling sensation, head sensation or heaviness, tiredness, drowsiness, dizziness, etc. Most of these symptoms have been minimal and actually are more common with other triptans than with Amerge. The symptoms usually are short-lasting. However, if they are more than mild, Amerge should not be taken again until you speak with your physician. We are careful with all triptans in patients who have major risk factors for heart problems. Amerge should not be used in people with hardening of the arteries or who have had past heart attacks. However, in all of the studies and previous experience with Amerge, it has generally been a safe medication.

How To Use Amerge Tablets

The earlier one uses any triptan, the better. Amerge, 2.5 mg. may be taken one every three to four hours, as needed, two in a day at most. Most patients have only needed one tablet. However, 5 mg., or two tablets in 24 hours, is the most that we want to use. The tablets are generally limited to 10 tablets per week at most. The very first time you use it, try ½ tablet to see how you will react.

Amerge With Other Medication

Amerge should not be taken in the same day as Imitrex, Migranal, Zomig, Relpax, Maxalt, or Axert. Pain medications (such as aspirin, Aleve, ibuprofen, Fiorinal, Vicodin, Tylenol, etc.) may be used, even at the same time as Amerge. This can increase efficacy. Anti-nausea medications may also be used at the same time. Generally, there are relatively few interactions with medications and Amerge.

How Long Does It Take To Work?

Amerge can take anywhere from 30 minutes to two hours to help. While Amerge does take somewhat longer to take effect, it lasts longer than most of the others in its class.

Instructions For Patients: Imitrex (Sumatriptan)

Imitrex is an extremely effective migraine abortive medication. Side effects have, in general, been found to be minimal. Imitrex is effective for approximately 70% of patients. The gold standard in headache abortive treatment. Imitrex tabs are now "fast-dissolving" in the stomach, leading to a quicker onset of action.

Who Should Use Imitrex?

Imitrex is excellent for migraine patients who are not at risk for coronary artery disease (CAD). Tablets of Imitrex can be used in patients in their 50's, or 60's, but with caution, and only in those patients who have been screened for CAD. Imitrex should not be a "last resort"; it is helpful for moderate as well as more severe migraines.

How To Use Imitrex Tablets

The earlier one uses any triptan the better the effect. Imitrex comes in 25 mg., 50 mg. and 100 mg. tablets. Most patients require 50 mg. or 100 mg. I start with 25 mg. (½ of a 50 mg.) every three to four hours, to assess how people will react to the drug. If they do not have adverse side effects, we have the patient take 50 mg., every three to four hours, up to a maximum of 200 mg. per day, or four of the 50 mg. tablets. Many patients will require 100 mg. per dose; all attempts are made, however, to minimize the dose.

How To Use Imitrex Nasal Spray

Imitrex Nasal Spray is available in 5 mg. and 20 mg. sizes. Each unit dose is for one-time use only. Almost all patients use the 20 mg. spray. Side effects are generally mild.

Patients should limit the nasal spray to two 20 mg. sprays per day at most, separating them by at least two hours. We use only one spray and two tablets in a day at most.

The nasal spray is very easy to use. The instruction sheet for patients is easy to follow; keep the head in an upright position, close one nostril, insert the nozzle of the nasal spray into the open nostril, and press the blue plunger on the Imitrex.

The nasal spray, of course, is very convenient. The nasal spray is usually sold in a box of six sprays at a time. A bad taste is the most common side effect. Keeping the head upright can help, do not lean the head back; patients have found that drinking a carbonated beverage prior to the spray, or sucking on a hard candy (particularly butterscotch) may alleviate the bad taste.

How To Use The Imitrex Injection

Imitrex injections are most often available in the STAT dose injector form, which is simple to learn and comes in a convenient hard case. This carrying case fits into a purse and renders transportation of the injections (which many patients do carry around with them) very easy. The injections are dosed at one every three to four hours as needed, but limited to no more than two in a day at most. The tablets are usually limited to ten tablets per week, and the injections to four per week. There are exceptions where we will use Imitrex daily for periods of time, particularly with cluster headaches. The vials of Imitrex, 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. Many patients prefer this route, and it allows the patient to use a lower (%) dose; this is effective for many people.

Mild Side Effects

Side effects are milder with the tablets than with the injections. Many people will not have side effects with Imitrex tablets. With the injections, they do often sense a “rush” into their head. Feeling heat in the head or numbness is relatively common. Chest heaviness or pressure, or pressure in the throat is also common. This is rarely from cardiac origin. If chest heaviness is moderate or severe, or is associated with arm pain, the patient should not use it again prior to clearance with the physician. Nausea is also common, as is fatigue, but these side effects tend to be short lasting. Most side effects resolve by 30 minutes.

Occasionally patients will feel weak or dizzy. Tingling in the fingers or feet may be experienced, particularly with daily high dose usage of Imitrex. Again, the tablets are usually much better tolerated (and convenient).

Serious Side Effects

The two serious side effects have been myocardial infarction and (possibly) stroke. Stroke has occurred in several cases, but it is unclear whether this was due to Imitrex or was a random event. Millions of people have had Imitrex now, and Imitrex has been used to treat over 350 million migraines. The issue of myocardial infarction and coronary ischemia is very important with the use of Imitrex. Imitrex does decrease coronary artery blood flow by approximately 17% for one hour or so. These effects are more marked with the injections than with the tablets. Patients at any age should be screened for coronary artery disease at least by history, and patients over the age of 40 should possibly have an appropriate workup (if indicated). The tablets have only been associated with rare cardiac events (out of tens of millions of doses given). However, in studies investigating Imitrex tablets, patients who have coronary artery disease or who have ventricular arrhythmias can have some ischemia. While Imitrex has generally been a very safe medication, it is important to screen these patients. After moderate or severe chest symptoms, it is prudent to discontinue use. Patients must be informed of possible adverse events.

Imitrex With Other Medication

Pain medications and OTC's (such as aspirin, Tylenol, Aleve, Vicodin, Fiorinal, etc.) are OK to use in the same day or even at the same time as Imitrex. This may enhance efficacy in some patients. Antiemetics such as Phenergan, Reglan, Compazine, etc. are safe with Imitrex. Midrin, which is a mild vasoconstrictor, should not be used within eight hours of Imitrex. While all indications are that they are probably safe, other triptans and Imitrex have not been cleared for use in the same day.

Imitrex With Pregnancy/Breastfeeding

Imitrex should not be used during pregnancy and should not be used by a woman who is nursing.

Other Uses Of Imitrex

Occasionally, Imitrex will be useful for preventing headache, particularly menstrual migraines. Sometimes we will use one tablet twice a day for three or four days for severe menstrual migraines. However, in general, Imitrex is too short-acting to be used as a preventative. Imitrex is also extremely effective in cluster headache and approximately 80% of cluster patients receive excellent relief from Imitrex. The longer-acting triptans, such as Amerge, may be better suited for prevention of headache.

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