

MEDICATIONS

While we are big advocates of non-drug treatments, many people do require the use of medications to control headaches. Headache medications are divided into two categories. Abortive drugs are those used as needed when the headache occurs. They are usually sufficient when headaches are infrequent. Prophylactic drugs are appropriate for people with frequent attacks, and they are taken daily to prevent headaches.

Pharmacological treatment for Tension-type headaches

Abortive therapy

Sporadic attacks of severe tension-type headaches may respond to analgesics.

- a. Non-steroidal anti-inflammatory agents such as ibuprofen (Motrin, Advil), naproxen (Naprosyn, Anaprox), aspirin or aspirin/acetaminophen/caffeine combination (Excedrin).
- b. Codeine or even stronger opioids may be required in a patient with occasional severe attacks. Chronic use of opioid analgesics in the treatment of headaches should be avoided.
- c. Drug combinations are often very effective for infrequent use. Combination of acetaminophen or aspirin with caffeine and a short acting barbiturate such as butalbital is very popular with many patients (Fiorinal, Fioricet, Esgic, Medigesic).
- d. Isometheptene, a sympathomimetic amine with vasoconstrictive properties is available in combination with dichloralphenazone, a mild sedative and acetaminophen (Midrin, Isocom). This combination can be effective in many patients who do not respond to other drugs. Drowsiness is a potential side effect. A limit of 15 to 20 tablets a month is placed on combination drugs or strong analgesics. If a patient takes more than that amount, the medication may begin to worsen the headache through a rebound mechanism. Such patients require prophylactic treatment.

Prophylactic therapy

Pharmacological treatment of severe persistent headaches begins with nortriptyline (Pamelor) or another tricyclic antidepressant (TCA). Detailed guidelines for the use of TCAs are provided in the chapter on peripheral neuropathies. Other antidepressants such as fluoxetine (Prozac), sertraline (Zoloft) and paroxetine (Paxil) can be effective with fewer side effects. Young women who constitute the majority of migraine sufferers often prefer the latter

group because these drugs, unlike TCAs, do not have a potential for weight gain and can even help them reduce weight.

Propranolol, nadolol and other beta blockers are less effective than TCAs in tension headaches but can be tried when other medications fail. Despite the fact that stress and tension are major causes of tension headaches use of tranquilizers should be avoided. Chronic use of these drugs can lead to addiction and worsening of headaches. Botulinum toxin (Botox) injections into pericranial muscles, which produce temporary (3 months) muscle paralysis are being tested as a prophylactic therapy for chronic tension headaches.

Pharmacological treatment for Migraine Headaches

Abortive therapy

Abortive therapy is used when the attacks are not very frequent.

a. Non-steroidal anti-inflammatory agents mentioned above can be effective for migraine headaches as well. Rapid onset of action can be achieved by using an effervescent form of aspirin (Alka-Seltzer).

b. Combination medications listed in the section on tension headaches can be very effective. Addition of codeine to some of the combinations (Fiorinal with codeine and Fioricet with codeine) improves their efficacy for severe headaches.

c. Ergots alone (Ergostat, sublingual) and with caffeine (Cafergot, tablets and suppositories, Wigraine, tablets) can be quite effective. These drugs can sometimes worsen or cause nausea. Reducing the dose, particularly of Cafergot suppositories to one quarter or one half of a suppository can avoid nausea and provide effective and rapid relief. Ergots are contraindicated in patients with cardiac or peripheral ischemia and pregnant women.

d. Dihydroergotamine (DHE-45) is effective for abortive treatment of migraines. This ergot derivative is available only in a parenteral form and can be given subcutaneously, intramuscularly or intravenously. A dose of 1 mg is sufficient for most patients but some may require 2 or 3 mg. The starting dose should be 0.5 mg repeated in 45 minutes if necessary. Once a total effective dose is established for a patient, that amount is given for future attacks. A nasal spray preparation of dihydroergotamine (Migranal) is more convenient to take, but it is less effective.

If the headache is accompanied by nausea an injection, a tablet or a suppository of prochlorperazine (Compazine) or tablet or injection of metoclopramide (Reglan) are usually effective. Triptans are a true breakthrough in the treatment of migraines. They are "designer" drugs

specifically developed to bind to 5HT_{1B,1D} serotonin receptors which are involved in the pathogenesis of migraine headaches. They relieve not only the pain, but also all the associated symptoms of a migraine. These drugs are not identical, therefore if one does not work or causes side effects another one in this group should be tried. Many patients respond to only one of the four or three out of four may cause side effects. Sumatriptan (Imitrex) was the first triptan on the market. Sumatriptan injection relieves both the pain and the nausea and allows the patient to return to normal functioning within 10-20 minutes. Sumatriptan is available in an injection which can be self-administered by the patient, a nasal spray and a 25 or 50 mg tablet. The nasal spray has a lower efficacy and consistency of response. The starting oral dose is 50 mg, the maximum single dose is 100 mg and daily up to 20 mg can be taken. Common side effects of an injection include a flushed sensation, paresthesias and injection site pain. Sumatriptan is contraindicated in patients with uncontrolled hypertension, ischemic heart disease or multiple risk factors for it and complicated migraines, i.e. migraines that are accompanied (not preceded, like in a migraine aura) by neurological deficits). Sumatriptan, other triptans and ergots should not be given on the same day. Zolmitriptan (Zomig) was the second triptan after sumatriptan to be introduced. It is possibly somewhat faster in onset and for some patients causes fewer side effects. The starting dose is 2.5 mg, which can be increased to 5 mg in a single dose and up to 10 mg in a day. It will be soon available in an orally disintegrating tablet, which obviates the need for water. This is useful when no water is available or when nausea and vomiting makes the patient through up even small amounts of water. Rizatriptan (Maxalt) is a triptan which probably has a faster onset of action than sumatriptan and is available in regular and rapidly disintegrating tablets. Patients often perceive the rapidly disintegrating tablets as quicker in onset, however, the pharmacokinetic tests indicate that their equal or the tablet is slightly faster because absorption does not occur in the mouth, but rather in the upper GI tract. Naratriptan (Amerge) is a triptan with the longest half-life and the slowest onset of action, which relegates it to the last place in the selection of triptans.

Prophylactic therapy

- a. Tricyclic and other antidepressants can be as effective for migraine headaches as they are for tension-type ones.
- b. Propranolol, nadolol and other beta blockers are good prophylactic drugs. The effective dose for propranolol can be as low as 40 mg daily but is usually 80 to 240 mg. Long acting preparation of propranolol (Inderal LA) facilitates its use. Contraindications for the use of beta blockers include bronchial asthma, sinus bradycardia, greater than first degree block, congestive heart failure, and diabetes.
- c. In some patients who do not respond to either a TCA or a beta blocker alone

use of these two drugs together may stop the headaches. No clinical trials have been published, however, to prove the efficacy of this combination.

d. Divalproex sodium (Depakote) can relieve migraine headaches in patients who do not respond to beta blockers or antidepressants. The starting dose is usually 250 mg a day with a gradual increase up to 2000 mg in a divided dose. Potential side effects include nausea, drowsiness and weight gain. Other anticonvulsants that can be useful in the prophylaxis of migraines are topiramate (Topamax) and gabapentin (Neurontin).

e. Calcium channel blockers are sometimes effective for migraines, but are more likely to benefit a patient with cluster headaches. NSAIDs can sometimes be effective for prevention of migraines. Botulinum toxin (Botox) injections into pericranial and cervical muscles can be effective in prevention of migraines with almost no side effects and the duration of the effect of 2-4 months. Magnesium was found to be effective in prevention of migraines in two placebo-controlled, double-blind studies. The dose is 400-600 mg a day of magnesium oxide or chelated magnesium (magnesium glycinate) taken every day with food. A single double-blind study suggests that a megadose (400 mg a day) of riboflavin can prevent migraines after 2-3 months of daily intake.

Pharmacological treatment for Cluster Headaches

Abortive therapy

Treatment of cluster headaches begins with measures designed to reduce pain of each attack while prophylactic drugs take effect.

1. The most benign and frequently effective treatment is inhalation of oxygen. It is done through a mask (not nasal prongs) using 100% oxygen at 8-10 liters per minute. It should be used for patients who get most of their attacks at home. If headaches occur during the day, patients can store another oxygen tank at work.
2. Sumatriptan (Imitrex) injection is very effective in most patients and has few side effects. It can also be self-administered by the patient using an auto-injector.
3. Ergotamine (Cafergot, Wigraine, Ergostat) can abort a cluster headache in up to 75% of patients. It is best given by a suppository or sublingually to provide rapid onset of action. Dihydroergotamine (DHE-45) is given only by injection and can be self-administered by the patient.

Prophylactic therapy

1. A short course of prednisone will frequently stop the cluster. Dosage is

started at 60-80 mg daily and then is tapered down over a period of two weeks.

2. Calcium channel blockers are suggested for patients not responding to a course of prednisone.

a. Nifedipine (Procardia) 40-120 mg daily, verapamil (Calan, Isoptin) 120-360 mg daily and nimodipine (Nimotop) 180-360 mg daily have can prevent cluster headaches in some patients.

b. Long acting preparations of nifedipine and verapamil allow for once-a-day dosage. Nimodipine has to be taken every 4 hours.

3. Methysergide (Sansert) in a dosage of 2 mg three or four times a day is recommended for patients who fail prednisone and calcium channel blockers. Fibrotic complications should not occur because clusters rarely lasts for more than a few months. However, some reports suggest that this complication is more likely to be idiosyncratic rather than dose-related.

4. Divalproex sodium (Depakote) 750-2000 mg daily in divided doses can provide relief for some patients as can topiramate (Topamax).

5. Lithium carbonate, 300 mg taken two to four times a day is effective within 1-2 weeks of therapy. It can work for both episodic and chronic forms of cluster headaches sometimes transforming chronic into episodic. Adding 2-4 mg of ergotamine a day to lithium may produce remission in patients who do not respond to lithium alone.

6. Ergotamine in a dose of 2 mg can provide good relief if taken 2 hours before the expected attack. Regular intake of 1-2 mg of ergotamine three times a day has been reported to be effective in some patients.

7. Over-the-counter melatonin, 10 mg nightly has been reported to help a few patients with clusters. Intranasal capsaicin has been also used to prevent clusters. It is applied into the nostril on the side of the headache.