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Acute treatment of migraine headache

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The purpose of this article is to provide practitioners with the tools necessary to diagnose and treat acute migraine. The current diagnostic criteria for migraine are outlined. Pearls to distinguish migraine from the other primary headaches, such as tension-type headache and cluster headache, are provided. The importance of the headache history, plus indications for neuroimaging, are presented. Readers will be taught how to take an effective headache history. General principles of treatment, including appropriate medication selection, medication dosing and route of administration, medication contraindications, drug interactions, and tips to optimize success are covered. A stratified care plan is outlined. Acute migraine treatment options are discussed, including dosing, side effects, and summary recommendations for simple analgesics, combination analgesics, opiates, corticosteroids, and the migraine specific ergots and triptans. The 7 available triptans are covered in detail and tips for selecting the most appropriate triptan for specific situations are delineated. Preventative and future treatments are briefly discussed.

Migraine affects approximately 12% of the population in most Western societies. The World Health Organization has shown that migraine is one of the top 20 disabling disorders. The burden of illness and cost for migraine is greater than that of epilepsy, stroke, Parkinson's syndrome, multiple sclerosis, and Alzheimer's disease combined.

The prevalence of migraine varies by age and sex. Before puberty, slightly more boys are affected than girls. As puberty and adolescence approaches, migraine prevalence increases rapidly in girls and, during the adult years, female migraine sufferers outnumber male ones by 3:1.[1] More than 80% of patients who develop migraine have their first attack before the age of 30 years.

The correct identification and diagnosis of migraine headache is essential. The International Headache Society (IHS) has published a second classification of headache disorders (the ICHD-2), in 2004. The primary headache disorders fall into 3 main categories: (1) migraine, (2) tension-type headache, and (3) cluster headache. Migraine is subclassified into migraine without aura, migraine with aura, basilar type migraine, hemiplegic migraine, and chronic migraine.

The IHS diagnostic criteria for migraine without aura require at least 5 previous attacks of headache lasting 4 to 72 hours. The headache must have at least 2 of the following 4 characteristics: unilateral location, pulsating quality, moderate or severe pain intensity, or aggravation by or avoidance of routine physical activity, such as bending over. In addition, during the headache, the patient must have at least one of the following 3 characteristics: nausea, vomiting, or both photo and phonophobia. An aura is classified as a fully reversible neurological symptom that develops gradually over greater than 5 minutes and lasts no longer than 60 minutes. A headache fulfilling the criteria for migraine with aura must begin during the aura or follow the aura within 60 minutes. Common auras include visual symptoms (flashing lights, blind spots, zig-zag lines, colored dots or loss of vision in certain areas), sensory symptoms (numbness or tingling in one side of the face, arm or leg), or speech

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Table 1 Migraine headache diagnostic criteria of the ICHD-2

Migraine without aura:
- A. At least 5 attacks fulfilling criteria B-D
- B. Headache attacks lasting 4-72 hours (untreated or unsuccessfully treated)
- C. Headache has at least two of the following characteristics:
  1. Unilateral location
  2. Pulsating quality
  3. Moderate or severe pain intensity
  4. Aggravation by or causing avoidance of routine physical activity (eg, walking or climbing stairs)
- D. During headache at least one of the following:
  1. Nausea and/or vomiting
  2. Photophobia and phonophobia
- E. Not attributed to another disorder

Typical aura with migraine headache:
- A. At least 2 attacks fulfilling criteria B-D
- B. Aura consisting of at least one of the following, but no motor weakness:
  1. Fully reversible visual symptoms, including positive features (eg, flickering lights, spots or lines) and/or negative features (ie, loss of vision)
  2. Fully reversible sensory symptoms, including positive features (ie, pins and needles) and/or negative features (ie, numbness)
  3. Fully reversible dysphasic speech disturbance
- C. At least 2 of the following:
  1. Homonymous visual symptoms and/or unilateral sensory symptoms
  2. At least one aura symptom develops gradually over ≥5 minutes and/or different aura symptoms occur in succession over ≥5 minutes
  3. Each symptom lasts ≥5 and ≤60 minutes
- D. Headache fulfilling criteria B-D for 1.1 *Migraine without aura* begins during the aura or follows aura within 60 minutes
- E. Not attributed to another disorder

disturbance. It is important to note that motor weakness is not included in this classification. Motor auras are in the separate category of hemiplegic migraine (Table 1).

When diagnosing migraine it is important to correctly distinguish it from the 2 other primary headache disorders, ie, tension-type headache and cluster headache. Tension-type headaches are the most common and prevalent type of primary headache, affecting 70% to 90% of the population. Tension-type headaches last from 30 minutes to 7 days. They have at least 2 of the following characteristics: bilateral location, pressing/tightening (nonpulsating) quality, mild or moderate intensity, no aggravation by routine physical activity. In addition, tension-type headache must have both of the following characteristics: no nausea or vomiting and no more than one of photophobia or phonophobia. Tension-type headache is a bilateral headache with none of the qualities of migraine (Table 2).

The rarest of primary headaches, and the only one that occurs more in men than women, is cluster headache, which affects <0.1% of the population. Cluster patients have severe, extremely intense, and unbearable unilateral orbital, supraorbital, and/or temporal pain lasting 15 to 180 minutes if untreated. Cluster headaches are accompanied by at least one of the following autonomic signs: ipsilateral conjunctival injection, lacrimation, nasal congestion, rhinorrhea, eyelid edema, forehead sweating, miosis, or ptosis. Many patients have a sense of restlessness or agitation during the attack and that may be used instead of any autonomic finding to qualify for the diagnosis. In addition, cluster headaches tend to be cyclical, coming in bouts about once per year for a 4- to 8-week cluster period. During that period patients have attacks from one every other day to 8 per day, often at the same time daily, and frequently waking the patient in the early morning. The presence of any autonomic symptom in a patient with a headache lasting about 1 hour should point to the diagnosis of cluster headache, and not migraine or sinus problems. The restlessness or agitation during a cluster attack contrasts with a migraine attack during which patients prefer to lie absolutely still in a dark quiet room.

Finally, it is of utmost importance not to miss serious and life-threatening causes of headache. Any headache that is the worst headache of the patient's life, of sudden onset (thunderclap headache), or presenting with marked changes (in frequency, location, accompanying neurologic symptoms or severity) should be investigated further with neuroimaging. We usually prefer the use of magnetic resonance imaging as the initial screening tool. In addition, patients with possible or proven HIV, cancer, seizures, or new onset headache after the age of 50 warrant further evaluation. Any patient with an abnormal neurological history or examination should be further evaluated.

Table 2 Tension-type headache diagnostic criteria of the ICHD-2

- A. At least 10 episodes occurring on <1 day per month on average (<12 days per year) and fulfilling criteria B-D
- B. Headache lasting from 30 minutes to 7 days
- C. Headache has at least two of the following characteristics:
  1. Bilateral location
  2. Pressing/tightening (nonpulsating) quality
  3. Mild or moderate intensity
  4. Not aggravated by routine physical activity, such as walking or climbing stairs
- D. Both of the following:
  1. No nausea or vomiting (anorexia may occur)
  2. No more than one of photophobia or phonophobia
- E. Not attributed to another disorder

Taking a headache history

The most important tool in diagnosing a headache is the history. When taking the history, key questions must be asked to correctly diagnose the type of headache disorder and to determine how much impact the headaches are having on the patient's life. This will be important in choosing the correct therapy according to a stratified care plan, in which we give the optimal treatment the first time. Crucial elements in the headache history are timing of the attack onset, pain location, duration, frequency, intensity, quality, associated features, aggravating/precipitating factors and ameliorating factors. Also important are the social, family and past history, especially previous medications and their efficacy. It is always good to note how many days in the past 3 months the patient has missed work, school, or familial obligations because of their headaches.[2]

Treatment of a migraine attack

Once the proper diagnosis of migraine headache is made, therapy can be instituted. Before prescribing medication, one should foster a therapeutic alliance with the patient. Most patients have not had this type of alliance with a care giver and will appreciate and benefit from it. Patients should understand that they need to participate in their own care, avoid migraine triggers, get regular sleep, meals, exercise, and avoid stress. It is also important to reassure the patient that, based on history, examination, and appropriate testing, no other serious pathology exists. Headache diaries/calendars are essential tools to help patients identify migraine triggers and track response to treatment.

Migraine treatment is divided into behavioral therapies (that will not be covered here), acute care, and daily preventive medication. The goal of acute care is to treat attacks early with optimal medications to effect rapid and consistent improvement to a pain free state without recurrence of the pain within the next 24 and preferably 48 hours. The best medication is one with the highest efficacy, the fewest adverse events, and the lowest cost. It is crucial to be familiar with efficacy, side effect profiles, drug-drug interactions, and the presence of coexisting conditions that might lead to certain contraindicated drugs when selecting the optimal treatment.

We recommend the use of migraine-specific agents (not analgesics) as first-line treatment when possible. The route of administration should be appropriate for the attack characteristics and patient preference. For example, if a patient has severe nausea, poor gastrointestinal (GI) absorption, or vomiting, an injection or nasal spray is ideal.

There are more than 40 different medications currently prescribed for acute care of migraine. Only 25% of these have approved indications by regulatory authorities. When choosing from the multitude of available medications, we recommend a stratified care approach—pick a medication with the highest potential efficacy and fewest adverse events—and use it from the start. This is as opposed to step care which requires the patient to start with the mildest medication to see if it works. We will present several categories of medication but still recommend starting with triptans or ergots from the start.

Simple analgesics

Some patients can successfully treat migraine by taking simple analgesics, such as aspirin, acetaminophen, or nonsteroidal anti-inflammatory agents. This is especially true if these agents are taken early in the course of the attack, the pain is mild, and no nausea or disability is present.[3] Aspirin, 500 mg p.o. may be effective. The main side effects of aspirin are bleeding and GI problems. Aspirin should not be given to children because of the risk of Reye's syndrome.

There is conflicting evidence in the literature about whether acetaminophen or aspirin should be the first-line agent for mild migraine treatment. They should be used cautiously in patients who drink alcohol. However, in patients who are pregnant, aspirin hypersensitive, or have contraindications to other medications, a trial of acetaminophen is warranted. Acetaminophen, 1000 mg p.o. is the suggested dose. Acetaminophen can cause liver toxicity in doses exceeding 4 g/d.

Nonsteroidal anti-inflammatory agents (NSAIDs) may be effective for the acute treatment of migraine.[4,5] Clinical studies have shown that diclofenac-K (50-100 mg), flurbiprofen 100 to 300 mg, ibuprofen 200 to 800 mg, naproxen sodium 550 to 1100 mg, piroxicam SL (40 mg), and tolfenamic acid (200-400 mg) are effective in the treatment of migraine.[4] In the office or emergency department, ketorolac 15 to 30 mg intravenously (IV) or 30 to 60 mg intramuscularly (IM) as well as diclofenac sodium IM are useful.[4] Other options include celecoxib 100 to 200 mg or indomethacin 25 to 50 mg.[6] Indomethacin is no longer available in a suppository form, but because it is so effective, one should consider having it compounded in a pharmacy. The side effects of NSAIDs include transient increase in blood pressure, GI disturbance, renal abnormalities, and heart failure.

Summary. Aspirin and NSAIDs may be effective in the acute treatment of occasional, mild migraine when taken early and in the absence of nausea. Acetaminophen is not a usual first line medication, but can be tried in patients who have contraindications to other medications, such as pregnancy.

Combination analgesics

Caffeine is an adenosine antagonist, a vasoconstrictor, and can work as an analgesic adjuvant in migraine. Many over-the-counter pain medications contain various combinations of caffeine, aspirin, and acetaminophen. Several prescription medications are combined with caffeine (ergotamine tartrate and the butalbital-containing medications). However, caffeine-containing preparations may produce medication overuse headaches and lead to transformed or chronic migraine and caffeine dependency. In fact, in doses

as small as 100 to 200 mg/d of caffeine (equivalent to drinking 1-2 6-oz. cups of coffee) several days a week can worsen headaches by causing caffeine withdrawal and rebound headaches. Caffeine overuse may also cause insomnia, palpitations, tremor, anorexia, nervousness, and tachycardia.

Summary. We do not recommend the use of combination analgesics for acute migraine treatment unless people can limit them to less than 4 days per month (because they may cause medication overuse headaches and lead to transformed migraine). In our practice, we gradually wean patients off all caffeine and then may let them use decaffeinated coffee, tea, or soft drinks and sometimes up to 1 cup of coffee per day. Remember to suggest the avoidance of sugar substitutes and artificial sweeteners in all beverages, as they can increase headaches, or trigger migraine attacks.

Opiate analgesics

Opiates have a limited therapeutic role in the treatment of migraine because they do not stop the migraine process and they produce more disability. They are not as effective as triptans in pain relief, disability, and side-effect profile. Parenteral opiates often are administered in the emergency department as rescue medications, when other medications might be more helpful. The main risks of opiates are sedation, cognitive dysfunction, constipation, and respiratory depression in high doses.

Summary. We do not recommend routine use of opiates for the acute treatment of migraine, but rare use when other medications have failed may be acceptable. Better choices in emergent settings are the IV medications outlined below.

Ergot alkaloids

Ergotamine tartrate. Ergotamine tartrate works on serotonin receptors and is a migraine-specific medication. Discovered more than 50 years ago, ergotamine tartrate is available in oral, sublingual, and rectal preparations. It used to be available as an injection and orally inhaled preparation. Before the availability of triptans in the 1990s, ergots were the vasoactive medications widely used for migraine therapy.

However, oral ergotamine tartrate is poorly and erratically absorbed. Bioavailability is less than 5% of the ingested dose. Rectal administration is slightly greater with better treatment efficacy.[7] Currently, the most commonly used preparations of ergotamine tartrate are tablets and suppositories. Tablets contain 1 mg of ergotamine tartrate and 100 mg of caffeine. Suppositories contain 2 mg of ergotamine tartrate and 100 mg caffeine. Because of the better rectal absorption of ergotamine tartrate, smaller doses should be given. Start with one quarter of a suppository and repeat in 1 hour if needed. The maximum dose of ergotamine is 4 mg/d. Do not use ergotamines more the 1 to 2 days/week to prevent ergotamine induced rebound headaches.

The side effects of ergotamine have limited its regular use in the therapy of acute migraine. Ergotamine usually worsens nausea and vomiting and could cause abdominal pain, paresthesias, and muscle cramps. Also, of great concern in headache patients is the development of ergotamine dependency and rebound headaches. This can be seen even when ergotamine tartrate is used as little as 2 d/wk. Given its vascular effects, ergotamine tartrate is contraindicated in patients with coronary artery disease, peripheral vascular disease, hypertension, pregnancy, sepsis, or liver and kidney disease. Ergotamine tartrate should not be administered with cytochrome P450 3A4 inhibitors (such as tetracyclines and antifungal drugs) as blood levels of the drug may rise causing serious adverse events.

Summary. Although effective as a migraine-specific medication, the use of ergotamine tartrate is limited by its side effect profile (especially nausea) and potential for rebound headaches. Ergotamine tartrate does not usually work as completely or as quickly as a triptan and is not a usual first line medication.

Dihydroergotamine. Dihydroergotamine (DHE) is a hydrogenated ergot preparation that has been available since the 1940s. DHE is more effective in the treatment of acute migraine than ergotamine tartrate. It is available in injectable and intranasal forms. It is given either IV, subcutaneously (SC), or IM by a physician or nurse. The patient may take the intranasal preparation at home. Although it is a weaker arterial constrictor and stronger venoconstrictor than ergotamine tartrate, it has the same side effect profile and contraindications as triptans.

In the nasal spray form, DHE 0.5 mg is sprayed into each nostril and should be repeated 15 minutes later for a total of 4 sprays (2 mg total dose). The nasal spray is usually well tolerated with the most common side effect of nasal stuffiness.

DHE can also be given IM or SC in a 1-mg dose. An antiemetic, such as PO or IM promethazine or prochlorperazine can be given concurrently but is not usually necessary. DHE is most effective in IV form but thus is much less convenient than oral triptans and more likely to produce nausea. However, it is highly effective and clinically appears to work well into a migraine attack, even if the patient has developed central sensitization and allodynia. The half-life of DHE is 10 hours, and it has an active metabolite, both of which may contribute to its long-lasting effect and low recurrence rate.

When IV DHE is indicated, the patient is hospitalized, and multiple doses are administered. The starting test dose is 0.25 to 0.5 mg given as a slow IV push over the course of 5 minutes. Patients usually are pretreated with an antiemetic. If no significant side effects occur, another 0.5 mg is given in 60 minutes. Repetitive doses of DHE 0.5 to 1 mg IV are administered every 8 hours over the course of 3 to 5 days. Dexamethasone 4 mg can also be given PO, IM, or IV concomitantly, although there is no good evidence in the

literature to support this, except in patients overusing medications.

Summary. DHE intranasally, SC, IM, and IV are all useful in the acute treatment of migraine. IV dosing is the most effective, but has practical limitations as most patients require hospitalization for repeated IV dosing. Antiemetics should be given concomitantly before each dose.

Triptans

Triptans are the most highly selective, migraine-specific, acute-care treatment currently used in the outpatient setting.[4,5,8] There are 7 different triptans currently available by tablet. In order of their clinical development and approval by the Food and Drug Administration (FDA), they are sumatriptan, zolmitriptan, naratriptan, rizatriptan, almotriptan, frovatriptan, and eletriptan. They are available in various strengths and formulations, including oral tablets, orally disintegrating tablets, nasal sprays, and SC injections. The clinical distinctions between these agents are slight, and choosing between them requires special attention to patient characteristics. Each patient seems to do better on one triptan than the others, but there is no way to predict the outcome for any patient. All 7 of the triptans are highly effective, so subtle differences in half-life, route of administration, onset of action, and side effect profile are important in the selection process.

The route of administration determines the onset of action of the triptans. Subcutaneous delivery of sumatriptan is the most rapid. Pain relief can begin as early as 10 to 15 minutes after SC injection. A high percentage of attacks are improved in 2 hours, but there is also a greater incidence of adverse events and a high recurrence rate.

Nasal spray is also very rapid and one study on zolmitriptan nasal spray shows the same 10-minute efficacy vs placebo that is seen with the sumatriptan injection. Sumatriptan and zolmitriptan are available in nasal spray form. Sumatriptan nasal spray begins to work in 15 minutes, but many patients do not like its taste. Zolmitriptan nasal spray has a more neutral taste, and begins to work in 10 to 15 minutes after administration. The intranasal route is convenient to use, and probably more effective if the patient is nauseated, and it is faster in onset than tablets. However, patients prefer tablets.

In addition to the route of administration, other factors to consider when choosing among the triptans are pharmacokinetic differences, duration of action, percentage of attacks achieving headache relief or a pain free state at 2 hours and frequency of recurrence. Sumatriptan is the oldest triptan medication and thus has been administered to the greatest number of patients. Zolmitriptan is the only triptan proven effective when repeated for a persistent headache. Naratriptan has a slower onset of action, but a longer half-life which can be helpful in patients with long-lasting or menstrually related migraine. Rizatriptan has the fastest response rate and highest 2 hour pain free rate of all the oral triptans. Almotriptan has a slightly better side effect profile than sumatriptan and has less reported chest pain as a side effect. Frovatriptan is a slow acting triptan, but has the longest half-life (26 h). Frovatriptan may also be helpful in patients with long-lasting or menstrually related migraine. Eletriptan is the newest triptan and works rapidly with a low recurrence rate.

Despite these differences, triptans are more similar than different, and one cannot predict which triptan will work best for any given patient.[7] Practitioners should make a calculated judgment as to which triptan is likely to be most effective and then systematically trial a second or third triptan whether the initial triptan does not work. Patients must be carefully questioned to determine whether the triptan they are taking is a good fit in rapid onset of action, complete response, minimal side effects, and lack of recurrence. If the patient has tried the same triptan at maximal doses for 2 migraine attacks without successful resolution of headache or intolerable side effects, another triptan should be trialed. If 2 or 3 triptan tablets have not worked, switching to nasal pray or injections is appropriate. Sometimes

Table 3 Triptan medications

Generic	Brand	Formulations	Doses	Maximum daily dose
Sumatriptan	Imitrex	Tablets	25, 50, 100 mg	200 mg
		Nasal spray	5, 20 mg	40 mg
		Subcutaneous injection	4, 6 mg	12 mg
Zolmitriptan	Zomig	Tablets	2.5, 5 mg	10 mg
	ZOMIG-ZMT	Orally disintegrating	2.5, 5 mg	10 mg
	Zomig NS	Nasal spray	5 mg	10 mg
Rizatriptan	Maxalt	Tablets	5, 10 mg	30 mg
	Maxalt-MLT	Orally disintegrating	5, 10 mg	30 mg
Naratriptan	Amerge	Tablets	1, 2.5 mg	5 mg
Almotriptan	Axert	Tablets	12.5 mg	25 mg
Frovatriptan	Frova	Tablets	2.5 mg	7.5 mg
Eletriptan	Relpax	Tablets	20, 40 mg	80 mg

Used with permission from The Triptan Formulations, CNS Drugs 17:434, 2003, Table 2.

DHE nasal spray or injection works when all triptans have failed.

Drug-drug interactions are also important to note when selecting a triptan medication. Sumatriptan, rizatriptan, and zolmitriptan should not be used with MAO inhibitor antidepressants. Rizatriptan requires a dose reduction to 5 mg in patients taking propranolol. The clearance of naratriptan is reduced with concomitant administration of oral contraceptives and in smokers. Zolmitriptan also may require a dose reduction in patients taking cimetidine or oral contraceptives. Eletriptan should not be used with CYP3A4 inhibitors.

All triptans stimulate serotonin 1-B and 1-D receptors. They are all vasoconstrictors and cause peripheral and possibly central arterial wall narrowing. Thus, patients with specific vascular risk factors should not take triptans. Contraindications to triptans are coronary artery disease, risk factors for coronary artery disease that have not been carefully evaluated, cerebrovascular disease, peripheral vascular disease plus hypertension that is not controlled, and cardiac conduction abnormalities. Risk factors include smoking, obesity, family history of early or severe coronary artery disease, diabetes mellitus, sedentary lifestyle, hypercholesterolemia, cerebrovascular disease, uncontrolled hypertension, and cardiac conduction defects. Triptans should be used cautiously in Raynaud's syndrome. Do not use triptans in patients with unusual or prolonged auras, basilar migraine, or hemiplegic migraine because of risk of stroke or other vascular insults. In the vast majority of patients triptans are very safe drugs. No single triptan has been shown to be safer than another.

The FDA approved a combination pill of sumatriptan 85 mg and naproxen sodium 500 mg in April 2008. In preliminary studies it has been shown to be more slightly more efficacious than either agent alone in the treatment of acute migraine. This combination tablet has the same side effect profile as the triptans and NSAIDs.

Summary. Triptans are the most highly selective, migraine-specific, acute-care treatment currently used in the outpatient setting and should be the first line medications in migraine patients who do not have coronary artery disease or other contraindications. All 7 of the triptans are highly effective, so subtle differences in half-life, route of administration, onset of action, and side effect profile are important in the selection process (Table 3).

Table 4 Preventative therapies

Alpha$_2$-agonists dose range	
Clonidine tablets	0.05-0.3 mg q.d.
Guanfacine tablets	1-3 mg q.d.
Membrane stabilizers (AEDs)	
Divalproex sodium tablets (extended-release available)	500-1500 mg q.d.
Gabapentin tablets and capsules	300-3000 mg
Pregabalin capsules	150-300 mg
Levetiracetam tablets	1500-3000 mg
Topiramate tablets	50-400 mg
Zonisamide capsules	100-400 mg
Antidepressants	
Monoamine oxidase inhibitors	
Phenelzine tablets	30-90 mg q.d.
Tricyclic antidepressants	
Amitriptyline tablets	30-150 mg q.h.s.
Nortriptyline tablets	30-100 mg q.h.s.
SSRIs	
Fluoxetine tablets	10-40 mg
Sertraline tablets	25-100 mg
Paroxetine tablets	10-40 mg
Venlafaxine tablets and XR form	37.5-225 mg
Mirtazapine tablets	15-45 mg
Beta-blockers	
Atenolol tablets	25-100 mg
Metoprolol tablets	50-200 mg
Nadolol tablets	20-200 mg
Propranolol tablets	30-240 mg
Timolol tablets	10-30 mg
Calcium channel antagonists	
Verapamil tablets	120-720 mg
Diltiazem tablets	90-180 mg
Nisoldipine tablets	10-40 mg q.d.
Amlodipine tablets	2.5-10 mg q.d.
NSAIDs for prevention	
Naproxen sodium tablets	500-1100 mg
Ketoprofen tablets	150 mg
Mefanamic acid tablets	1500 mg
Flurbiprofen tablets	200 mg
Rofecoxib (off the market)	12.5-50 mg
Celecoxib	100-200 mg
Valdecoxib (off the market)	10-20 mg
Serotonin antagonist agents	
Methysergide tablets (off the United States market)	2-12 mg
Methylergonovine tablets	0.2-0.4 mg t.i.d.
Cyproheptadine tablets	2-16 mg
Pizotifen tablets	1.5-3 mg
Miscellaneous	
Monteleukast sodium tablets	5-20 mg
Lisinopril tablets	10-40 mg
Botulinum toxin type A injection	50-150 Units (IM) q 3 mon
Namenda	5-20 mg
Magnesium glycinate tablets	400-600 mg
Riboflavin tablets	400 mg q.d.
Candesartan	8-32 mg
Quetiapine	12.5-200 mg

Corticosteroids

The mechanism of action of steroids for the acute treatment of migraine is not well understood but probably relates to their effect on perivascular neurogenic inflammation and possibly on central and peripheral sensitization thought to be involved in the pathogenesis of migraine. There is not much evidence in the literature to support the use of steroids in the acute treatment of migraine, but most headache specialists will use oral steroids as a rescue medication when the triptan medications have failed. There is some evidence to support the use of IV steroids in status migrainosus.[9,10] Steroids can also be helpful acutely when detoxifying patients from overuse syndromes. All steroids have side effects especially when used long term. These side effects

include hyperglycemia, mood disturbance, insomnia, weight gain, GI abnormalities, glaucoma, Cushing's syndrome, and osteoporosis. There are few serious side effects when used for just a few days. Steroids may also be one of the safest drugs to terminate migraine in a pregnant woman after the first trimester.

Summary. Although not well documented in the literature, oral steroids may be effective in the acute treatment of migraine when triptans have failed. IV steroids are also useful in status migrainosus.

Preventive treatment

Preventive medications are indicated in patients with more than 4 to 8 migraines/month, those with headaches more than 8 days per month, those with several days of disability per month, or who are poorly responsive to or cannot take acute care medications. Preventive medications should be chosen based on the patient's coexisting medical problems, such as depression, hypertension, or seizures or the contraindications due to possible drug-drug interactions. If the correct medication is chosen, the patient can benefit from a daily medication that works on both migraine and an underlying medical condition. Only 5 medications are FDA approved for the prevention of migraine. These are methysergide (which is no longer available in the United States), propranolol, timolol, divalproex sodium, and topiramate. However, many other classes of medications can be used off label. These include the beta-blockers, calcium channel blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, monoamine oxidase inhibitors, tricyclic antidepressants, selective serotonin reuptake inhibitors (should probably be avoided as they can increase migraine), serotonin norepinephrine reuptake inhibitors, other antidepressants, anticonvulsants, alpha 2 antagonists, nonsteroidal anti-inflammatory agents, and serotonergic type 2 agonist agents. Patients need to be given preventive medications at the optimal dose for at least 3 to 6 weeks for an adequate therapeutic trial. Most patients will need to remain on a preventative medication for 6 to 12 months or longer (Table 4).

Future therapies

MK-0974 (telcagepant) is an oral CGRP antagonist that is currently in phase 3 trials for the acute therapy of migraine. It appears to work as well as triptans, does not constrict blood vessels and has fewer side effects than triptans. Also in trials are a sumatriptan patch, orally inhaled prochlorperazine, loxapine and DHE, ketorolac nasal spray and a nitric oxide synthase inhibitor. Memantine (Namenda) is an Alzheimer's disease therapy that has been shown clinically and in open label trials to be helpful in migraine.

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