Information for Health Care Professionals

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How to Choose a Preventive Medication for Migraine

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Principles of Preventive Treatment

Daily preventive migraine therapy is indicated for patients with frequent migraines (once weekly or more), significant disability associated with individual attacks, contraindications to triptans and other vasoactive medications, significant triptan side effects, or use of symptomatic treatment more than 3 times weekly. Preventive medications should be chosen based on co-existing medical conditions, as the optimal medication may improve both the migraine and the medical condition. For example, consider a beta blocker or calcium channel antagonist for a migraine patient with hypertension; a tricyclic antidepressant taken at bedtime may benefit a migraine patient who is depressed or having difficulty sleeping. Other considerations include desirable and undesirable effects/side effects, as well as potential drug interactions with existing medications.

General principles of management:

- Always start treating with preventive medications at a low dose and gradually increase over an extended period of time.
- Continue well tolerated medications for at least 2-3 months at a therapeutic level before deciding on effectiveness.
- Communicate clear expectations regarding the timing and magnitude of expected clinical benefit.
- Warn patients of the most frequent adverse events and explain when to contact you.
- Establish a comprehensive migraine management plan that includes long-term goals, tips on when the medication needs to be changed, a regular office visit schedule, and guidelines for contacting the office.

There are only five FDA-approved medications for migraine prevention and one of them, methysergide, is off the market in the U.S. The others are **propranolol, timolol, divalproex sodium** and topiramate. It is best to stay on-label with these four medications when instituting migraine preventive therapy. But if they are not helpful or if they are contraindicated, you may need to resort to off-label uses of medications approved for other conditions.

The various categories of preventive medication are:

ß- Blockers

Propranolol, nadolol, atenolol, metoprolol and *timolol* are effective for migraine prevention. Common side effects are lethargy, depression, exercise intolerance, hypotension and sleep disorders. Avoid their use in patients with asthma, diabetes, bradycardia and congestive heart failure.

Calcium Channel Antagonists
Although not FDA-approved for migraine, over 45 clinical studies report on the efficacy of several different agents including: *verapamil, flunarizine* (not available in the United States), *nimodipine, nifedipine, cyclandelate*, and *nicardipine*. The most common side effects are constipation and edema. They are useful for basilar-type migraine and isolated aura symptoms.

Antidepressants
Four major types of antidepressants are available: monoamine oxidase inhibitors (MAOIs), selective serotonin re-uptake inhibitors (SSRIs), serotonin norepinephrine re-uptake inhibitors (SNRIs), and tricyclic antidepressants (TCAs). All have been used extensively for prevention of migraine, although they occasionally cause headaches to worsen. They are useful in patients with co-existing depression, anxiety, tension-type headache or primary stabbing headache. Serotonin syndrome has been reported in patients taking serotonin reuptake inhibitors with triptans but is rare; the incidence is approximately 0.03%. There is less experience using *buproprion* and *trazodone* for migraine prevention.

Membrane Stabilizers (Anticonvulsants)
Membrane stabilizers frequently used in the prevention of migraine include *divalproex sodium* (available and approved in an extended release form which is given only once per day), *sodium valproate, topiramate* and *gabapentin*. Several other medications in this category such as *levetiracetam* and *zonisamide* have shown promise as migraine preventive medications in open trials. *Valproate* is contraindicated in pregnancy, and should not be prescribed for women intending to become pregnant. Potential neural tube defects should be discussed with all women with childbearing potential taking *valproate. Topiramate* should not be prescribed for patients with a history of kidney stones.

Nonsteroidal Anti inflammatory Drugs
NSAIDs, often used in acute treatment, also can prevent migraine. A meta-analysis of seven placebo-controlled studies of naproxen (500 mg/day) or naproxen sodium (1100 mg/day) suggest a modest but clinically significant improvement in headache index and reduction in frequency. However, daily use of some NSAIDs may cause Medication Overuse (Rebound) Headache.

Vitamins, Minerals, Supplements and Herbs
Several over-the-counter preparations have been shown in randomized trials to be effective in migraine prevention in some patients. They are Feverfew (*Tanacetum parthenium*), Butterbur (*Petasites hybridus*), Magnesium, Vitamin B2 (Riboflavin), Coenzyme Q 10 and melatonin.

Serotonergic Agents
Methysergide
Methysergide (Sansert) has been used for migraine prevention for over 50 years but its use is limited due to its risk of retroperitoneal and peripleural fibrosis associated with extended use. It was discontinued from the US market in 2003, but it is still available in Canada.

Cyproheptadine
The antihistamine cyproheptadine is a 5-HT_2 antagonist with calcium channel blocking properties. Although its clinical efficacy has not been proven in double-blind, randomized studies, clinical experience suggests that it may confer some benefit in the prevention of migraine in children. It is not well tolerated by adults.

Miscellaneous Preventive Treatments

Botulinum toxin

Botulinum toxin type-A (Botox™) injections may be helpful in patients with migraine and other headache types, as well as in patients who are refractory to oral agents or do not tolerate them. It is not approved by the FDA for migraine prevention and many insurers require pre-authorization for coverage.

References

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