

From The Medical Letter on Drugs and Therapeutics

Prevention of Migraine

Patients with frequent or severe migraine headaches and those who cannot take vasoconstrictors or are refractory to acute treatment should receive preventive treatment.^{1,2} Menstrual migraine attacks may sometimes be prevented by a brief course of an NSAID or triptan, particularly frovatriptan or naratriptan, taken for several days before and after the onset of menstruation.^{3,4} Preventive therapy is generally not recommended during pregnancy.

Beta Blockers

Beta blockers are commonly used for prevention of migraine. Propranolol (Inderal LA, and others) and timolol are the only beta blockers approved by the FDA for this indication, but metoprolol (Lopressor, and others), nadolol (Corgard, and generics), and atenolol (Tenormin, and generics) are also effective in preventing migraine.² All beta blockers can cause fatigue, exercise intolerance, and orthostatic hypotension, and should not be used in patients with decompensated heart failure. All are relatively contraindicated in patients with asthma. Patients with migraine often have comorbid depression, which may be aggravated by beta blockers.

Pregnancy

Intrauterine growth retardation, small placentas, and congenital abnormalities have been reported with use of propranolol during pregnancy. Atenolol has been associated with the birth of small for gestational age infants and, at high doses, with embryofetal resorptions in animals.

Antiepileptic Drugs

Valproate (Depakote, and others) and topiramate (Topamax, and generics) are similarly effective in decreasing migraine frequency and are FDA-approved for migraine prevention. About 50% of patients achieve a $\geq 50\%$ reduction in headache frequency with these drugs.⁵ In randomized, double-blind trials, topiramate was at least as effective as propranolol for migraine prevention.^{6,7} Topiramate has reduced the number of migraine headache days per month and improved associated symptoms in patients with chronic migraine (≥ 15 headache days/month for ≥ 3 months) and medication overuse headache.^{8,9} In a trial in pediatric patients, however, topiramate was no better than placebo in preventing migraine.¹⁰

Adverse Effects

Adverse effects of valproate include nausea, fatigue, tremor, weight gain, and hair loss. Acute hepatic failure, pancreatitis, and hyperammonemia (in patients with urea cycle disorders) occur rarely. Other adverse effects include polycystic ovary syndrome, hyperinsulinemia, lipid abnormalities, hirsutism, and menstrual disturbances. Topiramate commonly causes paresthesias; fatigue, language and cognitive impairment, taste perversion, weight loss, and nephrolithiasis can also occur. Topiramate can rarely cause secondary narrow-angle glaucoma, oligohydrosis, and symptomatic metabolic acidosis.

Pregnancy

Use of topiramate or valproate during pregnancy has been associated with congenital malformations^{11,12}; neither drug should be used for migraine prevention in pregnant women.

Antidepressants

Amitriptyline is the only tricyclic antidepressant shown to be effective for migraine prevention in clinical trials,¹³ but it often causes sedation, dry mouth, and weight gain. Other tricyclics such as nortriptyline, which may have fewer adverse effects than amitriptyline, are frequently used for migraine prevention in adults. In a trial in pediatric patients, amitriptyline was no better than placebo in preventing migraine.¹⁰

The SNRIs venlafaxine (Effexor, and others) and duloxetine (Cymbalta, and generics) may also be effective in preventing migraine.^{14,15} They can cause nausea, vomiting, sweating, tachycardia, urinary retention, and increased blood pressure.

Pregnancy

Tricyclic antidepressant use during pregnancy has been associated with jitteriness and seizures in newborns. Fetal malformations are uncommon with SNRIs, but increased risks of neonatal behavioral syndrome and perinatal complications have been reported with use of SNRIs during pregnancy.¹⁶

Other Preventive Treatments

NSAIDs, such as naproxen and ibuprofen, have been used for prevention of migraine and for aborting acute attacks.¹⁷

The angiotensin-converting enzyme (ACE) inhibitor lisinopril (Prinivil, and others) and the angiotensin receptor blocker (ARB) candesartan (Atacand, and generics) have reduced migraine frequency by about 30-35% in small, double-blind trials.¹⁸ In a randomized, placebo-controlled, crossover trial, candesartan was noninferior to propranolol for prevention of migraine.¹⁹

The calcium channel blocker verapamil (Calan, and others) was somewhat more effective than placebo in some small studies.²⁰

The combination of simvastatin (Zocor, and others) and vitamin D was effective for migraine prevention in one small, randomized, placebo-controlled trial.²¹

The dietary supplement petasites (butterbur; Petadolex) 100-150 mg daily reduced migraine attack frequency by 36-60% in two randomized, placebo-controlled trials in about 300 patients,¹⁷ but it has been associated with hepatic toxicity.²² Melatonin, riboflavin, magnesium citrate, coenzyme Q10, and feverfew have also been effective in preventing migraine in small, randomized, placebo-controlled trials.^{17,22,23}

Pericranial intramuscular injections of onabotulinumtoxinA (Botox) are FDA-approved for prevention of headaches in adults with chronic migraine (≥ 15 headaches/month).²⁴ Botulinum toxin is not recommended for prevention of episodic migraine.

A transcutaneous electrical nerve stimulation device (Cefaly) that is worn on the forehead has been approved by the FDA for prevention of episodic migraine in adults. In one small study, daily 20-minute treatments for 3 months were modestly effective in reducing the number of migraine days per month.²⁵

ARTICLE INFORMATION

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