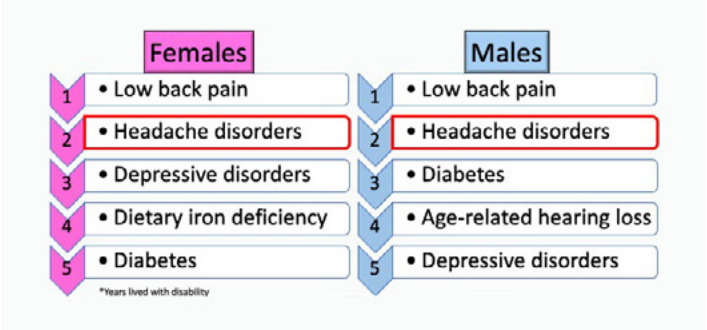
Clinical Insight

1. Burden of Disease

There are 3 broad groups of headache disorders, primary, secondary, and other. Common primary headache disorders include tension-type, migraine, and cluster. Headache disorders are the second leading cause of disability worldwide. The burden imposed by migraine on patients is enormous, but the burden imposed by cluster headache is even greater.

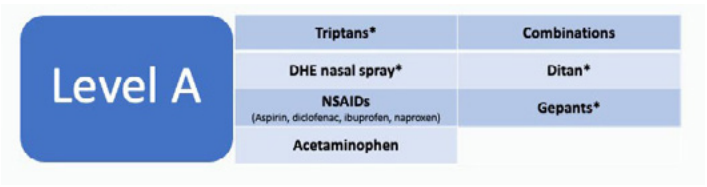


2. Screening and Diagnosis

Early identification of a primary headache disorder is important, thus routinely questioning patients about headaches and their use of nonprescription analgesics is imperative. Most patients who present to the clinic (not emergency department) for a headache disorder have a primary headache disorder. Tension-type headaches are generally relatively mild to moderate in intensity, compared with the moderate-severe and severe-very severe intensity in migraine and cluster, respectively. A careful history is essential to diagnosing a primary headache disorder. The physical examination in a patient with a primary headache disorder is usually normal, thus laboratory testing and imaging are not warranted unless there are red flag signs and/or symptoms. The International Classification of Headache Disorders, 3rd edition, is helpful to differentiate among primary headache disorders. Associated symptoms that distinguish untreated cluster headache from migraine headache are that patients with cluster often experience several short attacks over the course of a day and are typically agitated and restless, while the headache in patients with migraine typically lasts hours to a few days and patients seek a dark, quiet space. Patients with cluster exhibit autonomic features such as conjunctival injection, lacrimation, and/or nasal discharge, whereas patients with migraine are more likely to experience nausea and/or vomiting, photophobia, and phonophobia.

3. Acute Treatment of Migraine

Key receptors involved in the pathophysiology of migraine include serotonin-1B, 1D, and 1F, as well as calcitonin gene-related peptide (CGRP). A wide variety of medications have been used for acute treatment of migraine, but only a few are supported by good evidence and are approved for acute treatment of migraine. New targeted medications have been developed and are approved for acute treatment of migraine based on evidence from phase 3 clinical trials. These include the serotonin-1F agonist lasmiditan and the CGRP receptor antagonists rimegepant and ubrogepant. Patients who are candidates for a ditan or gepant include those who experience an inadequate response to triptans or older medications. Three neuromodulation devices have been cleared for the acute treatment of migraine in patients who experience an inadequate response to triptans, overuse standard treatment, or prefer nondrug therapy.



4. Preventive Treatment of Migraine

Preventive therapy is indicated in some patients with migraine, including those who experience significant morbidity or frequent attacks despite acute therapy. A wide variety of medications have been used for migraine prevention. Four CGRP receptor antagonist monoclonal antibodies have been approved for the preventive treatment of episodic and chronic migraine – erenumab, eptinezumab, fremanezumab, and galcanezumab. Analyses based on data from phase 3 clinical trials show that these CGRP monoclonal antibodies demonstrate a significant risk-benefit advantage compared with other evidence-based preventive medications. Patients who are candidates for preventive treatment with a CGRP monoclonal antibody are those with episodic or chronic migraine who experience an inadequate response to commonly used evidence-based preventive medications or demonstrate at least moderate disability due to migraine.

Lifestyle modifications to improve diet, exercise, and sleep, along with relaxation/meditation are recommended as standard components of migraine treatment. Adherence to treatment is suboptimal in most patients with migraine, thus identifying and addressing barriers to treatment adherence are important.

Medications for Preventive Treatment of Episodic Migraine	Level A: Effective	Level B: Probable
	Antiepileptics •Divalproex* •Valproate* •Topiramate* **β-blockers** • Metoprolol • Propranolol* • Timolol* **ARB** • Candesartan[1] **CGRP mAbs** • Erenumab* • Eptinezumab* • Fremanezumb* • Galcanezumab*	**SNRI/TCA** • Amitriptyline • Venlafaxine **β-blockers** •Atenolol •Nadolol

*Specifically indicated for migraine; all others are investigational
[1]Classified as possibly effective in original 2012 guideline; recent ev
of episodic migraine

5. Treatment of Cluster

In about half of patients with cluster headache, CGRP plays a key role in the pathophysiology. The high burden of cluster headache rests partly in the small number of evidence-based treatments that have been approved, eg, oxygen, dihydroergotamine, and subcutaneous sumatriptan. A noninvasive vagal nerve stimulation device has been cleared by the FDA for acute treatment of episodic cluster headache and as adjunctive preventive treatment of episodic and cluster headache. Galcanezumab is the only medication approved for preventive treatment of episodic cluster headache; injection site reactions are the most common adverse event.

6. Management Strategies

Shared decision-making is a process recommended to facilitate collaboration between the clinician and patient to make healthcare decisions that are the best for the patient. One shared decision-making model is the 5-step model developed by the Agency for Healthcare Research and Quality. MigrainePro is a patient-centered shared decision-making software application, developed by the National Headache Foundation, that shows patients how to analyze their migraine attacks and how to better implement acute treatment.