

Cluster Headaches

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Pathogenesis and Pathophysiology

The pathogenesis of cluster headaches has not been fully determined. Cluster events may be related to alterations in the circadian pacemaker, which may be due to hypothalamic dysfunction. Attacks increase following the beginning and end of daylight savings time, and there is a loss of circadian rhythm for blood pressure, temperature, and hormones, including prolactin, melatonin, cortisol, and beta endorphins. Neurogenic inflammation, carotid body chemoreceptor dysfunction, central parasympathetic and sympathetic tone imbalance, and increased responsiveness to histamine have been proposed as the cause of cluster pain.

Epidemiology and Risk Factors.

With an incidence of 0.01 to 1.5 percent in various populations, cluster headache prevalence is lower than that of migraine or Tension Type Headache (TTH). Prevalence is higher in men than in women and in black patients compared with white patients. The male-to-female ratio is about 6:1. A family history of cluster headache is rare. The most common form of cluster headache is episodic cluster. The rarest form is chronic cluster headache without remissions, with only about 10 percent of patients suffering from this variety of cluster. Cluster headache can begin at any age, but it generally begins in the late twenties. Cluster headache rarely begins in childhood, and only about 10 percent of patients develop cluster when they are in their sixties.

Clinical Features and Associated Disorders.

Patients with cluster headache have multiple episodes of short-lived but severe, unilateral, orbital, supraorbital, or temporal pain. At least one of the following associated symptoms must occur: conjunctival injection, lacrimation, nasal congestion, rhinorrhea, facial sweating, miosis, ptosis, or eyelid edema. Episodic cluster consists of headache periods of 1 week to 1 year, with remission periods lasting at least 14 days, whereas chronic cluster headache has either no remission periods or remissions that last less than 14 days.

The pain of a cluster attack rapidly increases (within 15 minutes) to excruciating levels. The attacks often occur at the same time each day and frequently awaken patients from sleep. If the condition is left untreated, the attacks usually last from 30 to 90 minutes, but may last up to 180 minutes. The pain is deep, constant, boring, piercing, or burning in nature, located

in, behind, or around the eye. It may radiate to the forehead, temples, jaws, nostrils, ears, neck, or shoulder. During an attack, patients often feel agitated or restless and feel the need to isolate themselves and move around. Gastrointestinal symptoms are uncommon. The attack frequency varies from one every other day to eight a day, occurring in cluster periods that last a week to a year. Remission between cluster periods generally lasts 6 months to 2 years. Most patients have one or two cluster periods a year that last 2 to 3 months, with one to two attacks per day.

Peptic ulcer disease is the only known associated medical disorder. Secondary cluster-like headache may occur due to structural lesions near the cavernous sinuses.

Differential Diagnosis. The differential diagnosis of cluster headache includes chronic paroxysmal hemicrania, migraine, trigeminal neuralgia (TN), temporal arteritis, pheochromocytoma, Raeder's paratrigeminal syndrome, Tolosa-Hunt syndrome, sinusitis, and glaucoma. Raeder's syndrome has characteristics similar to cluster headaches. It may be associated with severe pain, unilateral and supraorbital distribution, and an associated partial Horner's syndrome. It is distinct from cluster headache in that there are no distinct attacks and the pain is constant.

Evaluation. There are no studies that address the need for testing in cluster-like headache. In most cases, a careful history is all that is needed to make the diagnosis. MRI of the head is justified only in atypical cases or cases with an abnormal neurological examination (except when the abnormality is a Horner's syndrome).

Management. Patients with cluster headaches should avoid alcohol and nitroglycerin, yet other dietary and drug restrictions have little effect on cluster headaches. Pharmacological treatment for cluster headaches is divided into abortive and preventive therapy, and recommendations are mainly based on uncontrolled trials (Table 53-8). Oral preparations are absorbed slowly and are not recommended for the treatment of acute attacks. Effective abortive treatments that provide rapid onset of action include oxygen, sumatriptan, DHE, and (perhaps) topical local anesthetics. Inhaled oxygen, 7 to 10 L/min for 10 minutes following headache onset, is 70 percent effective and is often the treatment of first choice.

TABLE 53-8 -- CLUSTER HEADACHE PROPHYLAXIS

Drug	Dosage	Adverse Effects
<i>Episodic Cluster Headache*</i>		
Divalproex	500-3000 mg/day	Nausea, lethargy, tremor, weight gain, hair loss; rarely abnormal liver function, pancreatitis

TABLE 53-8 -- CLUSTER HEADACHE PROPHYLAXIS

Drug	Dosage	Adverse Effects
Ergotamine	Up to 4 mg/day	Nausea, paresthesia, intermittent claudication, ergotism
Lithium	300 mg bid or tid	Weakness, nausea, thirst, tremor, lethargy, slurred speech, blurred vision
Methysergide	2-14 mg/day	Muscle cramps, nausea, diarrhea, abdominal discomfort
Prednisone	40-100 mg/day,	Insomnia, restlessness, taper over 1-2 weeks personality changes, hyponatremia, edema, hyperglycemia, osteoporosis, myopathy, gastric ulcers, hip necrosis
Verapamil	120-720 mg/day	Constipation, edema, dizziness, nausea, hypotension, fatigue
<i>Chronic Cluster Headache</i> †		
Divalproex	500-3000 mg/day	Same as episodic
Lithium	300 mg bid or tid (0.4-0.8 mmol/L)	Hypothyroidism and polyuria
Methysergide	2-14 mg/day	Fibrotic reactions
Verapamil	120-640 mg/day	Same as episodic
*Begin early in the cluster period and continue until the patient has been headache-free for at least two weeks.		
† Combinations are often required.		
bid, twice daily; tid, three times daily.		

sumatriptan or DHE mesylate provide significant relief for about 80 percent of patients. An intranasal local anesthetic may provide relief for some patients.

Classification of Cluster Headache

According to its duration, the International Headache Society (IHS) classifies CH into episodic and chronic.

Episodic CH occurs in periods (clusters) lasting in duration from 7 days to 1 year, but separated by pain-free intervals lasting at least 2 weeks in duration. Typically, a cluster lasts 2 weeks to 3 months.

Chronic Cluster Headache

Chronic Cluster headache is defined as that occurring for more than 1 year without remission or without remissions lasting less than 2 weeks. It is subdivided into chronic CH from onset and chronic CH evolving from episodic. Chronic CH is notoriously difficult to treat and resistant to standard prophylactic agents.

Systemic cluster-like headache

Systemic cluster-like headache should be suspected if the presentation is atypical. Atypical features may include Absence of a periodic pattern Residual headache between exacerbations Incomplete or minimal response to standard therapy Presence of lateralizing findings on exam (except for those of CH-related Horner's syndrome)

Most patients with cluster headache require preventive treatment because each attack is too short in duration and too severe in intensity to treat with only abortive medication. In addition, ergotamine, DHE, sumatriptan, and oxygen may just postpone rather than abort the attack. Preventive therapy for episodic cluster, in order of preference, includes ergotamine, calcium channel blockers, methysergide, lithium, corticosteroids, divalproex, and capsaicin. Occasionally, indomethacin is effective. If medical therapy fails completely, surgical intervention may be beneficial for the psychologically stable patient with strictly unilateral chronic cluster. The surgery consists of neuronal ablation procedures directed toward the sensory input of the trigeminal nerve and autonomic pathways, and is generally effective in 75 percent. The prognosis of cluster headaches is guarded; it is a chronic headache that may last for the patient's life. Drug therapy may help convert some patients from chronic to episodic cluster.

Cluster headache is a vascular condition related to migraines. It relates to migraine in certain aspects of its pathogenesis and, consequently responds to some of the same medications. It differs from migraine in other aspects of its pathogenesis as well as in many aspects of its clinical presentation. Cluster headache is also, by far, not as common as migraine and, according to a population study, affects less than one out of 1,000 people. As opposed to migraine, it affects mostly men with a male to female ratio of at least 10 to 1. The age of onset of cluster headache is usually between 20 and 40 which is much later than in migraine. The clinical presentation of cluster headache is relatively easy to diagnose.

A trial of the Hinz amino acid method is worthwhile and highly effective for migraine headaches. It is also safe if followed according to professional protocol. Its value in cluster headaches has not been verified due to the fact that the latter are more uncommon than ordinary migraines.

