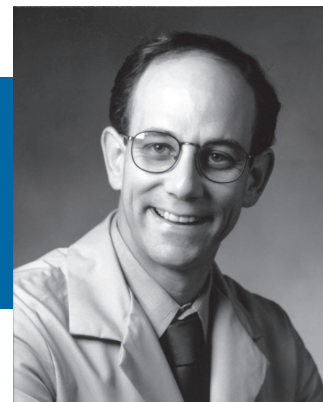


Preventive Therapies for Cluster Headaches

Lawrence Robbins, MD



Cluster headache is among the most severe pains known to mankind. It is characterized by excruciating, debilitating pain lasting from 15 minutes to 3 hours, and occasionally longer. The pain is usually located around or through one eye, or on the temple. The series of cluster headaches lasts several weeks to several months, and can occur once or twice per year, every other year, or even less frequently. Cluster headaches tend to occur more in the spring and fall.

Characteristics

Cluster headaches occur more frequently in men than women (2.5:1 ratio). Approximately 1 out of every 250 men have cluster headaches. The age of onset of cluster headaches is usually between age 20 and 45, but there are cases of cluster headaches occurring in teenagers, and occasionally the headaches begin after age 50, though rarely after 70 years of age. Women tend to have an older age of onset than men. There is usually no family history of cluster headaches, but occasionally cluster headaches do run in families.

The pain of the cluster attack is extreme and starts very quickly, usually without an aura or a warning. Within minutes, it becomes very severe. Although the pain is usually located about the eye or temple, it may be more intense in the neck or facial areas. Usually unilateral, the pain does change sides in 10% to 15% of patients, either during a cluster cycle, or at the next cycle. The pain itself is excruciating, described as sharp, stabbing, and even “like my eye is being pulled out.”

The length of headache attacks varies, but 45 minutes is the average. Cluster headache patients usually experience 1 or 2 headaches per day, but this may increase to as many as 7 headaches occurring in 24 hours, or decrease to as little as 1 or 2 attacks per week. The attacks usually occur around the same time each day, with the time period between 9 PM and 10 AM being most frequent. Approximately 50% of patients report being woken by the headaches. Several of the following symptoms are usually present at the time of the attack: lacrimation, nasal congestion, rhinorrhea,

conjunctival injection, ptosis, miosis of the pupil, or forehead and facial sweating. Nausea, bradycardia, and general perspiration also occur in many patients.

Table 1. Typical Characteristics of Patients with Cluster Headaches

- Begins between ages 20 and 45, approximately 0.4% of the population
- Male predominance in a 2.5 to 1 ratio
- Same time of year with no headache between the cluster cycles
- Primarily nocturnal attacks (but may be anytime)
- During a cluster cycle, alcohol triggers the headaches
- Severe, excruciating, unilateral pain—usually periorbital
- Ipsilateral rhinorrhea, lacrimation, conjunctival hyperemia, sweating of the forehead, Horner’s syndrome

Case History

Richard is a 40-year-old man with a history of 4-weeklong cycles of cluster headaches, occurring once a year in the fall. The headaches began when he was 35. The cluster period begins slowly, increasing over one week’s time and reaching a peak where Richard has 2 or 3 severe attacks per day. These occur during the night from 10 PM to 3 AM. Each cluster attack lasts from 40 to 90 minutes, and the pain is severe. The headache is always on the right side, and is accompanied by eye tearing and nasal congestion.

Examination and Treatment Plan

Richard visits our office during the first week into his 4-week headache series. The headaches are increasing in intensity and he is miserable from the pain. At this point, we

want to put Richard on a prophylactic regimen, and give him an abortive to help ease the acute attack. We decide to use prednisone, one 20-mg tablet in the morning and another with dinner (40 mg/day) for 4 days. We will reduce this to 20 mg/day after the first 4 days, and then to 10 mg/day after another 6 days. We will then taper off the prednisone entirely over the next 4 to 6 days.

Limiting the amount of corticosteroids is important for two reasons: 1) serious side effects are decreased, and 2) if necessary, we may want to utilize additional prednisone later in the cluster series. If the patient has been on a high-dose of steroids for 3 weeks, we cannot use more corticosteroid. In contrast, by keeping the amount to a minimum, we are able to use steroids later in the cluster period. Cluster sufferers may be more prone to femoral head necrosis with the use of corticosteroids.

With the prednisone, we begin a slow release form of verapamil. This is started at 240 mg/day; we may eventually increase to 2 doses per day, which is generally the maximum (480 mg/day). As the prednisone dose is decreased, and the patient is weaned off the medication, it is hoped that the verapamil will have taken effect.

The use of oxygen as an abortive is discussed with Richard, but he prefers to wait. We give him sumatriptan tablets, 100 mg, as he is reluctant to self-inject sumatriptan. Richard is also instructed to apply ice to the areas of pain. (See Table 2 for list of the most common preventative agents prescribed for cluster headaches.)

Results

Six days later, Richard calls the office. He has had 5 very good days, but as the prednisone is being decreased, the headaches are becoming more severe. Sumatriptan tablets do not help; last night, he had 90 minutes of extremely intense pain. At this point, we convince Richard to try oxygen, at 10 to 13 L/min,



as needed, and he rents a tank. Richard also is given sumatriptan injections, 4 mg.

We continue the original plan of decreasing prednisone, and we increase the dose of verapamil to 480 mg/d. We will monitor Richard's blood pressure. He now has oxygen and sumatriptan injections available as abortive agents; adding lithium or valproate are considerations, as is indomethacin.

I see Richard 4 days later. He is now in his third week of clusters, and by his previous pattern, has 1 to 2 weeks left in the cycle. However, at times a cluster period may exceed the previous one in length, and extended cluster periods of up to several months do occur. Richard states that the oxygen does help his headaches.

The clusters are less severe, but still occur regularly twice a night. Sumatriptan injections stop the attacks within 10 minutes of administration. The verapamil may be having some effect as well. He is down to 20 mg/day of prednisone, and we decide to taper off the dose over the next 4 days. If the headaches increase dramatically, he could return to the prednisone.

Six days later, the headaches are gone, and after a week without headaches, Richard is tapered off the verapamil over the course of 6 days. If the headaches were to return during those 6 days, we would immediately increase the dose of verapamil to the maximum of 480 mg, and consider using prednisone again.

Discussion

It is important to chart which medications are most effective for treating a patient's cluster headaches, so as to be ready to use them for the next cluster series. I usually write the plan for the next series in the patient's chart, and inform the patient of the plan.

In Richard's case, we would use oxygen as an abortive, with injections of sumatriptan. As a preventive, he would be given verapamil, increasing to 480 mg/day, and approximately 2 weeks of prednisone. Instead of the injections, zolmitriptan nasal spray would be a consideration, and occipital nerve blocks are a reasonable possibility. Other preventives would include lithium, indomethacin, sodium valproate or topiramate.

Most patients with cluster headaches are prescribed both preventative and abortive therapies. An in-depth overview of abortive therapies can be found in the July/August 2010 issue of *Practical Pain Management*. Compared to migraine management, we have relatively few medications that are effective for the treatment of cluster headaches. In order to minimize the use of corticosteroids, it is important to initiate preventative medications early in the cluster cycle. For the typical episodic cluster cycle, we begin medication with the onset of the cluster, and discontinue all medication shortly after the cycle ends. ■

Author's Bio:

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Table 2. Common Preventive Medications for Cluster Headaches

Class/Agent	Dosage	Side Effects	Comments
Corticosteroid: Prednisone	20 to 40 mg/d for 3 to 6 days, then taper off over 4 to 8 days.	Corticosteroids have many adverse effects. When used for short periods of time, the most common side effects are insomnia, gastrointestinal (GI) upset, and anxiety. Serious adverse events have occurred with even short courses of corticosteroids.	Very effective for cluster headache, prednisone is used primarily for episodic cluster headaches. It is given for 1 to 2 week duration during the peak of the cluster series. Additional steroids may be given later in the cycle, when the cluster headaches increase. Higher doses may be needed when the cluster cycle is peaking in intensity. Due to adverse side effects, it is very important to minimize the use of corticosteroids.
Calcium Channel Blockers: Verapamil ER	At onset of headache, 240 mg/d or bid—maximum dose 480 mg/d	Constipation. Electrocardiogram (ECG) should be performed because of possible cardiac abnormalities when higher doses are used.	Very effective in episodic and chronic cluster headaches. Often initiated at the onset of the headache, in conjunction with prednisone. Verapamil is then continued while the prednisone is tapered and then stopped. Because of its efficacy and minimal side effects, verapamil is a mainstay of cluster headache prevention.
Lithium	300 mg/d to 900 mg/d	Well-tolerated at low doses; drowsiness, mood swings, nausea, tremor, and diarrhea may occur.	Helpful for chronic cluster, and to a lesser degree, episodic cluster headaches. It may be combined with verapamil and/or prednisone. Blood tests need to be performed to assess kidney and thyroid function
Non-steroidal Anti-inflammatory Agents (NSAIDs): Indomethacin	25 mg/d or bid; up to 75 mg bid or tid.	GI side effects may limit use.	Powerful NSAID, indomethacin can be helpful for some cluster headache patients.
Anti-Epileptic Agents: Sodium Valproate	500 mg/d to 1500 mg/d	May cause weight gain, fatigue, and GI upset, among other side effects.	Valproate and topiramate are occasionally effective against cluster headaches. They are the mainstay of treatment against migraines, but less effective against cluster headaches.
Topiramate	50 mg/d to 200 mg/d	Does not cause weight gain, but cognitive side effects may limit use.	
Botulinum Toxin A Injection	50 to 200 units	Safe, usually no adverse effects; may cause eye droop, or (rarely) generalized weakness.	Botulinum toxin type A is FDA-approved for chronic migraine. While the injections are not as effective for cluster headaches, they do help to prevent cluster recurrences in some patients.
Occipital Injection: Corticosteroid	20 to 40 mg	local site reaction, or systemic corticosteroid effects (see above).	May decrease cluster headache occurrence for up to 4 weeks.
Bupivacaine	2 to 5 mL	Allergic reactions may occur (rare)	May decrease cluster headache occurrence for up to 4 weeks.