

# Pearls & Oy-sters: Trigeminal autonomic cephalalgias

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The trigeminal autonomic cephalalgias (TACs) are a group of primary headaches that are characterized by unilateral pain, a relatively short duration of symptoms, and associated ipsilateral cranial autonomic symptoms, such as Horner syndrome, lacrimation, and nasal congestion. Incidence is rare when compared to other primary headache disorders but diagnosis (and, more importantly, treatment) can prove to be a challenge even when presented with a typical clinical presentation. The TACs are listed in the International Classification of Headache Disorders (ICHD-II) under their own section and include the following<sup>1</sup>:

1. Cluster headache (CH)
2. Paroxysmal hemicrania (PH)
3. Short unilateral neuralgiform headache with conjunctival injection and tearing/cranial autonomic symptoms (SUNCT/SUNA)

See the table for a summary of treatment options.

**CLUSTER HEADACHE Pearl.** All cluster headaches need to be treated with abortive, transitional, and preventive therapies.

**Oy-ster.** The average time it takes for a patient with CH to be correctly diagnosed is 6.6 years. The average number of physicians seen prior to correct diagnosis is 4, and the average number of incorrect diagnoses prior to a diagnosis of CH is also 4.<sup>2</sup>

CH has a very typical clinical presentation and for this reason, the aforementioned “oy-ster” is unacceptable as patients suffer needlessly. Cluster sufferers will attest to thoughts of suicide, as the pain is extremely severe, and CH is often dubbed a “suicide headache.”

CH comes in 2 epidemiologic forms. Episodic cluster, the more common form, is characterized by attacks that occur daily during a cluster period, the period of attacks generally lasting 1–3 months, and followed by months or even years of remission before recurring. In chronic cluster, attacks occur for more than 1 year without remission, or with remissions lasting less than 1 month.<sup>1</sup>

Attacks are strictly unilateral with associated ipsilateral cranial autonomic features, and can be discerned from migraine by 2 key factors: 1) attack duration is less than the 4 hour minimum duration of a migraine attack according to ICHD-II criteria (CH attacks last 15–180 minutes); and 2) restlessness is present in CH attacks. Migraine attacks are accompanied by avoidance of movement; CH attacks by pacing and other manifestations of agitation.

When an attack of CH or another TAC occurs, the posterior hypothalamus is activated, causing a disruption in the connections for sleep. Thus, CH attacks frequently wake patients out of sleep.<sup>3</sup> Finally, the clinician should not be distracted by migrainous symptoms—photophobia can occur in 91% and phonophobia in 89% of CH attacks, and nausea occurs frequently in cluster as well.<sup>4</sup>

All CH sufferers need more than one acute treatment for attacks in case one fails. Because of the abruptness of the attack and its severity, as well as the short duration, oral medications should be avoided—they are too slow.

An extremely effective treatment to terminate a cluster attack is 6 mg of subcutaneous sumatriptan, achieving relief in 74% of patients within 15 minutes of onset vs placebo, and this formulation and dosage is Food and Drug Administration–approved for cluster.<sup>5</sup> Sumatriptan nasal spray at 20 mg has also been shown to be effective in randomized controlled trials, and 5 mg zolmitriptan nasal spray has also demonstrated efficacy vs placebo.<sup>5</sup>

All patients should be given a portable 100% oxygen tank for acute treatment, and O<sub>2</sub> becomes the first line therapy if triptans are contraindicated. A non-rebreather mask is used at a flow rate of 7–15 L for 20 minutes and can be repeated safely without issue.<sup>5</sup> Other effective abortive treatments include IV, IM, or subcutaneous dihydroergotamine, possibly intranasal lidocaine, and blockade of the ipsilateral greater occipital nerve.<sup>2,5</sup>

Many patients will present with a sense that a cluster cycle or period is beginning, and will know

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*Disclosure:* Author disclosures are provided at the end of the article.

**Table** Treatment recommendations for trigeminal autonomic cephalalgias listed in order of preference<sup>2,5,7</sup>

Type of treatment	Cluster headache	Paroxysmal hemicrania	SUNCT/SUNA	Hemicrania continua
<b>Abortive</b>	1) 7–15 L of O <sub>2</sub> for 20 min; plus 2) SC sumatriptan 6 mg; 3) NS sumatriptan 20 mg; 4) NS zolmitriptan 5 mg	Indomethacin 25–75 mg 3 times a day titrated to pain relief	Not needed	1) Indomethacin 25–75 mg 3 times a day to pain relief then taper; 2) celecoxib 200–300 mg twice a day; 3) naproxen 500 mg twice a day
<b>Preventive</b>	1) Verapamil 240–960 mg/d; 2) divalproex sodium 500–1,000 mg/d; 3) topiramate 50–100 mg/d; 4) lithium 300–1,200 mg/d; 5) melatonin 3–12 mg qhs	1) Verapamil 240–360 mg/d; 2) acetazolamide 250 mg 3 times a day; 3) botulinum toxin A	1) Lamotrigine 100–300 mg/d; 2) gabapentin 800–2,700 mg/d; 3) topiramate 50–75 mg/d; 4) carbamazepine	1) Lamotrigine 25–200 mg/d; 2) gabapentin 1,200–1,800 mg/d; 3) lithium 300–900 mg/d; 4) melatonin 3–9 mg qhs
<b>Transitional</b>	1) Prednisone 80 mg/d with decrease q3d by 20 mg for 2 wk; 2) dexamethasone 4 mg twice a day × 1 wk, then every day × 1 wk; 3) ergotamine tartrate 2 mg qhs or twice a day × 2 wk; 4) DHE 1 mg IM every day or twice a day × 2 wk; 5) occipital nerve blockade	Not needed	Not needed	Not needed
<b>Refractory procedures</b>	1) Sphenopalatine ganglion blockade; 2) radiofrequency thermocoagulation; 3) alcohol injection into supraorbital or infraorbital nerves, or trigeminal ganglion	None reported	Hypothalamic stimulation	None reported

Abbreviation: SUNCT/SUNA = short unilateral neuralgiform headache with conjunctival injection and tearing/cranial autonomic symptoms.

when attacks are starting. This is an excellent time to begin prophylactic therapy, which should be increased quickly but carefully until the majority of attacks have ceased. Otherwise, prevention is added as soon as the patient notes the cluster period has begun. Prevention might not be needed if at the end of a cycle.

The mainstay of preventive therapy is verapamil. It is typically tolerated up to 480 mg a day, although higher doses can be necessary. Patients can experience constipation, palpitations, peripheral edema, hypotension, and bradycardia. It is recommended that patients have an EKG with each significant increase in dosage.<sup>6</sup>

Because verapamil has significant side effects at higher doses, and because tachyphylaxis tends to occur with monotherapy, many headache specialists use a second preventive at the initial onset of treatment. Other drugs that can be effective include lithium, divalproex sodium, gabapentin, topiramate, methysergide, and, occasionally, melatonin (for episodic CH), or nasal capsaicin.<sup>7–10</sup>

Transitional treatment should be provided on the first visit while preventive medications are initiated, typically for 1–2 weeks. Corticosteroids can be used, beginning with 60–80 mg of prednisone daily and tapered by 20 mg every 3–4 days. Ergotamine tartrate at 2 mg or dihydroergotamine injection at 1 mg daily can be used effectively as well but preclude use of triptans for 24 hours after use.<sup>5</sup>

### PAROXYSMAL HEMICRANIA AND SUNCT/SUNA Pearl.

All patients with suspected PH or

SUNCT/SUNA need to have an MRI of the brain with and without gadolinium.

**Oy-ster.** Patience with the patient is necessary as multiple medications may need to be tried before finding one that is effective.

PH and SUNCT/SUNA are characterized by multiple daily attacks of unilateral head pain with cranial autonomic features. As with cluster, PH comes in 2 forms: an episodic form, in which attacks occur in periods lasting 1–3 months followed by times of remission and recurrence; and a chronic form without a month of remission during a year. Chronic PH is more common.

Attacks of PH last 2–30 minutes, and occur more than 5 times per day at least half the time. Attacks can be differentiated from CH in that they are shorter, 50% of patients will not experience the restlessness that comes along with CH, and the patients may not be awakened from sleep. PH occurs more often in women; CH in men.

The best diagnostic marker for PH is the excellent response to indomethacin. We typically begin 25 mg of indomethacin 3 times a day and increase every 2–3 days until 75 mg TID is reached (if needed). This should be tapered every so often to see if remission has occurred, as the natural progression of PH is largely unknown.<sup>7</sup> Other medications reported with occasional success include verapamil, celecoxib, acetazolamide, lithium, oxygen, ergotamine, and prednisone.<sup>11</sup>

SUNCT/SUNA is similar to PH but attacks last only 5–240 seconds (average 10–60 seconds) with up to 200 attacks per day.

Whereas CH, PH, and hemicrania continua (HC) occasionally occur without autonomic symptoms, SUNCT/SUNA attacks are defined by these features.<sup>11</sup> SUNCT/SUNA can be differentiated from trigeminal neuralgia (TN) by the V<sub>1</sub> distribution (<10% of TN), the absence of triggers, the higher frequency of attacks per day, and the presence of autonomic symptoms.<sup>11</sup>

SUNCT and SUNA may be refractory to treatment. Because the attacks are so short, therapy must be preventive. Lamotrigine (especially for SUNCT) and gabapentin (especially for SUNA) are the 2 most efficacious medications reported, but topiramate, intranasal lidocaine, corticosteroids, and IV phenytoin have been used as well.<sup>12</sup>

Imaging of the brain is required when suspecting PH or SUNCT/SUNA, as there are secondary causes that when treated, may resolve these conditions. Reported MRI findings of cerebellopontine angle tumors, prolactinomas, meningiomas, venous angiomas in the brainstem, lacrimal gland retention cysts, and brainstem infarctions have all been described as causing secondary TACS, with pituitary tumor resection occasionally associated with cure.<sup>11</sup>

**DIFFERENTIAL DIAGNOSIS Pearl.** Hemicrania continua is a unilateral headache with similar autonomic symptoms but is constant and responds well to indomethacin.

**Oy-ster.** Cervicogenic headache can be a mimicker of HC, particularly in the elderly.

HC is a continuous, unilateral, moderate level side-locked headache with severe exacerbations of variable duration manifesting at least one ipsilateral cranial autonomic symptom. HC is probably much more common than originally thought and often misdiagnosed.<sup>2</sup>

HC can also be accompanied by idiopathic stabbing headache, often called “jabs and jolts,” and is frequently associated with an ipsilateral foreign body sensation in the eye, like an eyelash or grit.<sup>13,14</sup> MRIs of the brain are mandatory during the workup, as secondary HC has been reported, often with etiologies similar to secondary PH and SUNCT/SUNA.

Response to indomethacin is a diagnostic marker in HC, as with PH.<sup>15</sup> Other medications occasionally reported as successful include other nonsteroidal anti-inflammatory drugs, gabapentin, lamotrigine, corticosteroids, dihydroergotamine, lithium, and melatonin.<sup>11</sup>

Cervicogenic headache can mimic almost any headache, especially a TAC, and should be considered when there is lack of response to treatment. Unilaterality of pain, radiation from the neck, and

failure to meet ICHD-II criteria for primary headaches can suggest cervicogenic headache as an alternative diagnosis to a TAC. Occipital nerve blocks can be helpful in cervicogenic headache, with physical therapy for maintenance, although Sjaastad et al. suggested controlled C2–3 blocks for diagnosis.<sup>16</sup>

## DISCLOSURE

Dr. Whyte reports no disclosures. Dr. Tepper serves on scientific advisory boards for Merck, GlaxoSmithKline, MAP Pharmaceuticals, Inc., NuPathe, and Zogenix; has received funding for travel from GlaxoSmithKline, MAP, Merck, NuPathe, and Zogenix; serves as an Associate Editor of *Headache*; receives royalties from the publication of *Conquering Daily Headache* (Decker, 2008) and *Understanding Migraine and Other Headaches* (University of Mississippi Press, 2004); has received honoraria from GlaxoSmithKline, MAP, Merck, NuPathe, Zogenix, Scienta Health, PriMed, the American Headache Society, and the Diamond Headache Foundation; has served on speakers' bureaus for GlaxoSmithKline and Merck; has received research support from GlaxoSmithKline, MAP, Merck, NuPathe, and Zogenix; and has reviewed records for Allergan, Inc.

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