

## OCCIPITAL NERVE STIMULATION FOR CHRONIC CLUSTER HEADACHE\*

Based on a presentation by David W. Dodick, MD†

### ABSTRACT

The greater occipital nerve has been implicated in the pain associated with cluster headache. Prophylactic medication is ineffective for a significant number of patients with chronic cluster headache and previous treatment options have consisted of ablative procedures carrying the potential for significant neurological morbidity. Greater occipital nerve stimulation may represent a safe and effective treatment option for chronic medically refractory cluster headache and warrants further study.

Cluster headache often manifests with severe pain, but most patients can be effectively treated with currently available medications. However, between 15% and 20% of these patients develop chronic cluster headache that is refractory to medical management.

Treatment options in severe chronic cluster headache cases have included neurolytic or ablative surgery involving the trigeminal or autonomic pathways using radiofrequency, glycerol rhizotomy, and even trigeminal nerve section at the brain stem level. Although sometimes effective, these procedures are invasive, are associated with a significant recurrence rate, and carry the potential for significant neurological morbidity.

(*Adv Stud Med.* 2003;3(6C):S569-S571)

### **RATIONALE**

The genesis of cluster headache may reside in the inferior periventricular hypothalamus. Morphometric magnetic resonance imaging and positron emission tomography (PET) studies in cluster headache patients and controls show both structural and anatomical differences. Specifically, activation in the periventricular hypothalamus is seen in patients with cluster headache but not in patients with migraine or experimentally induced first trigeminal division pain.<sup>1-3</sup>

Because occipital nerve blockade has been reported to be effective for short-term control, and deep brain (hypothalamic) stimulation for chronic pain has been successful, occipital nerve stimulation for chronic medically intractable cluster headache has recently emerged as a possible treatment option. One such case is reported here.

### **PATHOPHYSIOLOGY**

The trigeminal vascular system is felt to be closely involved in the pathophysiology of migraine and cluster headache. Significant elevations of calcitonin gene-related peptide (CGRP), a neuropeptide marker for the trigeminal system, can be measured in the cranial venous effluent of cluster headache patients during attacks.<sup>4</sup>

Nociceptive afferents that supply the vessels and dura through the first division of the trigeminal nerve (V1) and terminate in the medullary dorsal horn are believed to represent the anatomical substrate for pain in a variety of primary headache disorders. These nociceptive afferents also extend into and terminate in the C1 and C2 levels of the spinal cord dorsal horn. This dorsal horn area is where cervical afferents, particularly from C2, synapse. This "trigeminal cervical com-

\*Based on a presentation given by Dr Dodick at the 14th Migraine Trust International Symposium.

†Associate Professor of Neurology, Department of Neurology, Mayo Clinic, Scottsdale, Arizona.

Address correspondence to: David W. Dodick, MD, Department of Neurology, Mayo Clinic Scottsdale, 13400 East Shea Boulevard, Scottsdale, AZ 85259. E-mail: dodick.david@mayo.edu.

plex” accounts for the coexistence of facial and occipital-nuchal pain reported by many patients with chronic headache, including migraine and cluster headache.<sup>5</sup>

In addition, stimulation of cervical nerve roots and the greater occipital nerve, which is primarily C2-derived, refers pain to the periorbital region. Electrical stimulation of C2 and the superior sagittal sinus converge on the dorsal horn at C2, further suggesting a functional as well as anatomical continuum between nociceptive trigeminal and upper cervical afferents.<sup>5</sup>

### **GREATER OCCIPITAL NERVE STIMULATION**

Evidence from animal models indicate that stimulation of the greater occipital nerve inhibits stimulus-evoked trigeminal activity as measured by a significant reduction in CGRP in the cranial venous effluent on the side ipsilateral to the stimulation.<sup>6</sup> Greater occipital nerve stimulation also enhances the physiological response (excitability) of neurons within the trigeminal cervical complex to stimulation of nociceptive dural afferents. Again, this suggests a physiologic as well as an anatomical continuum between nociceptive trigeminal vascular and upper cervical nociceptive afferents.<sup>7</sup>

Italian researchers reported that 5 patients became cluster free after implantation of a stimulating electrode in the area of hypothalamus activation previously identified with PET studies. Onset of effect was either immediate or delayed up to 4 months after implantation, and no side effects were reported during a follow-up from 6 to 26 months.<sup>8</sup>

Occipital nerve stimulation has also been used in 13 patients with either occipital neuralgia or chronic migraine. Stimulating electrodes were implanted superficial to the cervical muscle fascia over the greater occipital nerve at the C1 level. Over a 2-year follow-up period, 8 patients reported greater than 75% pain relief, 4 reported greater than 50% pain relief, and 1 had the system removed upon complete pain resolution.<sup>9</sup>

### **OCCIPITAL NERVE BLOCKADE**

Based on this background, several investigators have tried occipital nerve blockade in patients with chronic cluster headache. In one study, which included 20 patients with either intractable episodic or chronic cluster headache, injection of lidocaine and methylprednisolone acetate arrested headache attacks for up to 17 days.<sup>10</sup> In another study including 10

patients, betamethasone injected around the greater occipital nerve arrested pain in 6 of the patients for up to 23 weeks.<sup>11</sup>

More recently, a group of 14 patients, 5 with chronic and 9 with episodic cluster headache, were treated with lidocaine 1% with 40 mg triamcinalone around the greater occipital nerve on the side ipsilateral to the pain. Nine patients had a good or moderate response and remained pain free for more than 2 weeks or 1 to 2 weeks, respectively. The overall mean pain-free response was 13 days.<sup>12</sup> These reports suggest that occipital nerve blockade can at least temporarily decrease the frequency of cluster headache attacks or arrest attacks for a short period of time.

### **CASE STUDY**

A 45-year-old man with a history of episodic cluster headaches since age 20 years presented with a 2-year history of chronic cluster headache. During this 2-year period, he was experiencing 4 to 5 attacks daily. The attacks were predominantly (90%) right-sided, and pain was primarily periorbital with occipital pain preceding or occurring during some cluster attacks. All conventional cluster headache prophylactic medications failed for this patient, and he was taking high doses of gabapentin, topiramate, lithium carbonate, and morphine sulfate at the time of consultation.

The patient failed to respond to a 3-day hospital course of repetitive intravenous infusions of methylprednisolone and dihydroergotamine. Blockade of the right greater occipital nerve resulted in a 3-day pain-free period. A second occipital nerve block resulted in a pain-free interval of 1 week before cluster headache attacks resumed. A decision was made to try an occipital nerve stimulator. After 5 days of unilateral right occipital nerve stimulation, the patient experienced only 1 left-sided cluster headache during a 2-week interval. Bilateral Pisces Quad leads were then placed over each occipital nerve. The patient experienced a 90% reduction in attack frequency over a 5-month period, tapered all prophylactic and opioid medication, and recognized the ability to quickly abort an attack within 5 minutes after identifying its onset. Approximately 7 months after the procedure, the patient began to experience suboptimal control. The pulse width, frequency, and amplitude of stimulation were adjusted; the stimulation paradigm was switched from intermittent to continuous stimulation; and

divalproex sodium 1000 mg was added. Twelve months after the procedure, the patient remains free of cluster headache.

## CONCLUSION

Occipital nerve stimulation in patients with medically refractory chronic cluster headache may represent a viable alternative to ablative or destructive trigeminal nerve procedures, and further study is warranted. Several questions remain unanswered, including the durability of this approach and whether occipital pain is required to obtain benefit. Furthermore, the need to confirm a temporary response to occipital nerve blockade before stimulator implantation requires further study.

## REFERENCES

1. May A, Bahra A, Buchel C, Turner R, Goadsby PJ. Functional magnetic resonance imaging in spontaneous attacks of SUNCT: short-lasting neuralgiform headache with conjunctival injection and tearing. *Ann Neurol*. 1999;46(5):791-794.
2. May A, Bachra A, Buchel C, Frackowiak RS, Goadsby PJ. Hypothalamic activation in cluster headache attacks. *Lancet*. 1998;352(9124):275-278.
3. May A, Ashburner J, Buchel C, et al. Correlation between structural and functional changes in brain in an idiopathic headache syndrome. *Nat Med*. 1999;5(7):836-838.
4. Goadsby PJ, Edvinsson L. The trigeminovascular system and migraine: studies characterizing cerebrovascular and neuropeptide changes seen in humans and cats. *Ann Neurol*. 1993;33(1):48-56.
5. Angus-Leppan H, Lambert GA, Michalicek J. Convergence of occipital nerve and superior sagittal sinus input in the cervical spinal cord of the cat. *Cephalalgia*. 1997;17(6):625-630.
6. Vincent MB, Ekman R, Edvinsson L, Sand T, Sjaastad O. Reduction of calcitonin gene-related peptide in jugular blood following electrical stimulation of rat greater occipital nerve. *Cephalalgia*. 1992;12(5):275-279.
7. Bartsch T, Goadsby PJ. Stimulation of the greater occipital nerve induces increased central excitability of dural afferent input. *Brain*. 2002;125(pt 7):1496-1509.
8. Leone M, Franzini D, D'Amico D, et al. Deep brain stimulation in posterior hypothalamic gray matter to relieve intractable chronic cluster headache. *Cephalalgia*. 2002;22:582.
9. Weiner RL, Reed KL. Peripheral neurostimulation for control of intractable occipital neuralgia. *Neuromodulation*. 1999;2(3):217-221.
10. Anthony M. Headache and the greater occipital nerve. *Clin Neurol Neurosurg*. 1992;94(4):297-301.
11. Raskin NH. Cluster headache. In: Raskin NH, Appenzeller O, eds. *Headaches*. New York, NY: ChurchillLivingstone; 1988:99.
12. Peres MFP, Stiles MA, Siow HC, Rozen TD, Young WB, Silberstein SD. Greater occipital nerve blockade for cluster headache. *Cephalalgia*. 2002;22:520-522.