

Brief Communication

Hemicrania Continua May Respond to Repetitive Sphenopalatine Ganglion Block: A Case Report

X. Michelle Androulakis, MD, MSc; Kaitlin A. Krebs, BA; Avi Ashkenazi, MD

Background.—Hemicrania continua (HC) is a chronic headache disorder characterized by a continuous, strictly unilateral head pain accompanied by cranial autonomic symptoms, which completely responds to indomethacin; however, few alternative treatment options exist for the patients with this disorder who cannot tolerate indomethacin. Sphenopalatine ganglion (SPG) block has been used for the treatment of various headaches, with the strongest evidence for efficacy in cluster headache.

Case Report.—A 52-year-old woman with a 7-year history of HC was evaluated in our clinic for management of her headaches after she had stopped using indomethacin due to a bleeding gastrointestinal ulcer. After failing multiple pharmacologic therapies, she was treated with repetitive SPG blocks using bupivacaine (0.6 mL at 0.5%) twice a week for 6 weeks and followed by maintenance therapy. This treatment protocol resulted in significant improvement in her headaches, mood, and functional capacity.

Conclusion.—SPG block using a local anesthetic may be an effective treatment for patients with HC, specifically for those who cannot tolerate indomethacin, or when this drug is contraindicated.

Key words: hemicrania continua, sphenopalatine ganglion block, cranial autonomic symptoms, trigeminal autonomic cephalalgias, indomethacin, chronic migraine

Abbreviations: CH cluster headache, HC hemicrania continua, NSAIDs non-steroidal anti-inflammatory drugs, SPG sphenopalatine ganglion block, TAC trigeminal autonomic cephalalgia

(*Headache* 2016;56:573-579)

INTRODUCTION

Hemicrania continua (HC) is a primary headache disorder classified as a trigeminal autonomic cephalalgia (TAC) and characterized by a continuous, strictly unilateral head pain associated with prominent ipsilateral cranial autonomic symptoms

as defined in ICHD III beta.¹ Similar to other TACs, the pathogenesis of HC is believed to involve facilitation of the trigeminal autonomic reflex, causing an increased cranial parasympathetic outflow through the sphenopalatine ganglion (SPG).² This chronic condition is completely responsive to indomethacin; however, long-term use of indomethacin carries the risk of developing gastrointestinal or renal adverse effects, which may

From the School of Medicine, Department of Neurology, University of South Carolina, Columbia, SC, USA (X.M. Androulakis and K.A. Krebs); Department of Medicine (Neurology), Doylestown Hospital, Doylestown, PA, USA (A. Ashkenazi).

Address all correspondence to M. Androulakis, University of South Carolina School of Medicine, Department of Neurology, Columbia, SC 29203, USA.

Accepted for publication October 23, 2015.

Conflict of Interest: Avi Ashkenazi and Kaitlin Krebs do not report any conflicts of interest. Michelle Androulakis discloses that she is currently funded by a grant sponsored by Tian Medical at the time of this manuscript submission; however, the grant was applied after the case manuscript was written and this author did not receive any financial or non-financial compensation for the creation/publication of this manuscript.

necessitate discontinuation of the drug.³ Attempts to wean off of indomethacin in patients with HC usually result in headache recurrence.

Blocking of the SPG using local anesthetics has been used in the treatment of headaches for decades.^{4,5} Recently, there has been increased interest in this treatment modality, which resulted in the development of new devices for this purpose.⁶⁻⁹ One of these devices, the Tx360[®], is considered to be a minimally invasive technique for SPG blockade and has been reported to provide significant pain relief for patients with trigeminal neuralgia and post-herpetic neuralgia.¹⁰ Additional treatments, such as electrical neuromodulation of the SPG, have emerged as a potential therapy for patients with refractory cluster headache (CH) and migraine.^{11,12} Here, we report a case of HC treated successfully with a series of SPG blocks using the Tx360[®] device.

CASE PRESENTATION

A 52-year-old white female, with a history of anxiety, presented to our outpatient headache clinic for the management of her chronic headaches. She had been diagnosed with HC seven years prior to her presentation. She took an early retirement from her job as a physician due to her disabling headaches. She has a history of several types of headaches, first presenting with migraine with aura in 1982. Her migraine attacks were characterized by a visual aura, photophobia, and right sided headache in the orbital, frontal, and temporal areas. Attack frequency was initially once per month, but subsequently increased to once a week. She tried numerous preventive and acute headache medications, with some improvement; however, since starting topiramate in 2007, her migraine has been in remission.

A different type of headache developed in 1996, after a whiplash injury was sustained during a motor vehicle accident. This headache manifested as severe pain at the right posterior neck and occipital region, occurred several times a week, was triggered by prolonged sitting at the computer, and lasted for approximately a day. This led to the diagnosis of cervicogenic headache. She was

unresponsive to treatment with non-steroidal anti-inflammatory drugs (NSAIDs), and could not tolerate acetaminophen with codeine. Baclofen was started in 2010, and has been helpful.

She also reported on a transient post concussive headache after a fall, lasting for about a week, in August 2007. Four months later she woke up with a continuous, right peri- and retro-orbital pain after having had wine for dinner. This headache was associated with agitation, photophobia, phonophobia, nausea, and vomiting. She also reported on parasomnias (hypnogogic/hypnopompic hallucinations) and sleep paralysis almost nightly with this headache. These symptoms lead to a diagnosis of cluster migraine. She tried numerous treatments for this headache, with little benefits. The headache stopped abruptly on December 8, 2007.

In April of 2008, she developed yet another type of headache. It had a continuous component originating in the superior-medial aspect of the right orbit, and spreading anteriorly and inferiorly to the maxilla and upper teeth. Pain intensity ranged between 3 and 7/10, and was accompanied by tearing, redness of the membrane adjacent to the inner canthus, nasal congestion, miosis, and ptosis, all on the right. She also had occasional abrupt, short jabbing headaches, which started in the right medial upper orbital region, radiating deep into the orbit, and extending into the right nasal septum and palate. These jabs lasted up to 10 seconds, were at intensity of 6-7/10, and accompanied by the same autonomic symptoms noted above (therefore excluding a diagnosis of primary stabbing headache). The clinical features of this headache were typical of HC.

In July of 2008, indomethacin was started, with significant improvement in her HC. She was then seen at a major headache center where the indomethacin dose was titrated up to 100 mg tid, with further clinical improvement and complete resolution of her headaches; however, the drug had to be stopped in 2010 due to a bleeding gastrointestinal ulcer. She also tried high dose melatonin (30 mg qhs), which resulted in nightmares, and therefore the dose was decreased to 10 mg qhs. Brain and cervical spine MRI with and without contrast, as

well as MRA of the head and neck with and without contrast were unremarkable.

As for the treatment of her other headaches, topiramate was discontinued due to cognitive impairment; however, her migraine has been in remission. Other failed treatments included several triptans, ergots, barbiturates, opioids, antiemetics, corticosteroids, benzodiazepines, calcium channel blockers, beta blockers, NSAIDs, anticonvulsants, tricyclic antidepressants, serotonin/norepinephrine reuptake inhibitors, angiotensin receptor blockers, muscarinic receptor antagonists, phenothiazine, and various supplements. She had undergone several inpatient infusion therapies and a variety of cranial nerve blocks (occipital, infraorbital, supraorbital, supratrochlear, and anterior auricular). An occipital nerve stimulator was implanted in 2011, with temporary headache improvement that lasted for about two years. She received onabotulinumtoxinA injections (four treatments) with no significant headache improvement. Her preventive medications at presentation were: gabapentin, lamotrigine, metoprolol, and melatonin. She was taking ketamine nasal spray and ondansetron as needed for pain and nausea.

Given the contraindication for indomethacin treatment in this patient, we decided to try SPG blockade as a treatment for her HC.

METHODS

The patient underwent a total of 12 SPG blocks with the Tx360[®] device, using 0.5% bupivacaine (0.6 mL) for 6 weeks (twice per week) on the symptomatic side. This was followed by maintenance treatment every 4-5 weeks.

She was asked to maintain a daily headache diary throughout the treatment and follow-up period. In this diary, the patient was asked to record the following for each day: her pain intensity three times per day, associated symptoms, and medications used. The pain intensity was measured based on numeric rating scale (NRS) for pain, with 0 representing “no pain” and 10 representing the “pain as bad as you can imagine” and “worst pain imaginable.” Each week these scores were averaged to yield average pain intensity for that week.



Fig. 1.—Improvement in ocular signs with SPG block therapy. At week 3 (top), at week 4 (middle), and week 6 (bottom). Note that the top image was taken at a dimmer light condition than the other pictures to better demonstrate the miosis in the patient’s right eye.

Headache Impact Test (HIT-6) and Patient Health Questionnaire-9 (PHQ-9) were administered using the standard questionnaire form and scored using each questionnaire specified guidelines.^{13,14}

The patient signed a consent form for this case report; she also signed a photo release consent form to allow us to use her photos presented in Figure 1.

RESULTS

The patient’s HC headaches responded favorably to SPG blocks using bupivacaine. Her response to treatment is summarized in Table 1. This clinical observation suggests that repetitive SPG blocks using local anesthetics may be an effective treatment for HC, specifically for patients who cannot tolerate indomethacin, or when this drug is contraindicated. While we did not observe an acute effect of SPG block on HC pain, repetitive blocks over several weeks proved effective. Overall, there was a reduction in both the average intensity of her continuous headache, and the frequency and

Table 1.—Frequency and Average Intensity of Headache Symptoms Over Time

	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 10	Week 14
Continuous HA								
Frequency (days/week)†	Daily	Daily	Daily	2	5	None	None	None
Average Intensity‡	6/10	5/10	3/10	1/10	1/10	None	None	None
Jabs/jolts								
Frequency (days/week)†	Daily	Daily	Daily	4	3	2	3	3
Average Intensity‡	7/10	7/10	5/10	3/10	1/10	1/10	1/10	1/10
Photophobia								
Frequency (days/week)†	4	3	3	1	None	None	None	None
Inability to function								
Frequency (days/week)†	2	1	1	None	None	None	None	None
Ptosis/nasal congestion								
Frequency (days/week)†	6	6	6	3	1	None	None	None
Response to ketamine spray§	Minimal	Minimal	Mild	Moderate	Moderate	Did not use	Did not use	Did not use
HIT-6	72					46		38
PHQ-9	10					3		2

HIT-6 = Headache Impact Test - 6; PHQ-9 = Patient Health Questionnaire.

†Frequency was recorded in the patient's daily headache diary.

‡Intensity was determined by a pain intensity numeric scale with "0 = no pain and 10 = worst pain you have experienced"; These scores were average for the days where either a continuous headache or jabs/jolts occurred.

§Response to ketamine spray was based on the patient's subjective report.

severity of her jabs/jolts. There was also a decrease in the severity of her photophobia and ptosis over the course of 14 weeks of treatment (Table 1). There was a 36% reduction in her HIT-6 score by week 4 and a 47% reduction by week 14, compared to baseline. In addition, when compared to baseline, there was a 70% reduction of her PHQ-9 score by week 4 and an 80% reduction by week 14.

DISCUSSION

SPG blockade has long been used for headache treatment.¹⁵ In earlier reports, blocking of the SPG was achieved using cocaine.⁴ Later on, lidocaine was used for this purpose, given its more favorable safety profile. Since the SPG has a major role in cranial parasympathetic outflow, it has been hypothesized that modulating the activity of this ganglion may be effective in the treatment of headaches associated with prominent cranial autonomic symptoms.¹⁶ Based on this notion, SPG blockade has been most commonly used for patients with CH.¹⁷ The efficacy of SPG blockade for CH has been shown in a number of studies.^{18–22} In those studies, SPG blockade was performed by delivering a local anesthetic to the

ganglion intranasally using various techniques (eg, spraying, dropping, or local application via a long cotton swab). More recently, several new devices (SphenoCath[®], Allevio[®], and Tx360[®]) have been developed which facilitate a more accurate and effective delivery of the local anesthetics to the SPG.^{6,7,23} SPG modulation using other techniques, such as electrical stimulation, chemical neurolysis, microvascular decompression, and surgical or radiofrequency ablation, has also been performed for a variety of head pain conditions.^{24–27} However, these interventions may be associated with significant adverse effects.

SPG block has been used for the treatment of migraine, with some evidence for efficacy.²⁸ In addition, there are anecdotal reports for the efficacy of this treatment in patients with some secondary headaches (eg, post-dural puncture headache, post-traumatic headache, and post-herpetic neuralgia).^{29–31} Interestingly, however, data as to the efficacy of SPG block in HC are scarce. Given some shared clinical features and underlying pathogenesis between HC and CH, and the evidence for efficacy of SPG block in the latter, it can be speculated that blocking the SPG may be beneficial in HC as well.

Our patient's response to this treatment supports this notion, which needs to be further examined.

The exact mechanism of action of SPG modulation for headaches remains to be elucidated. It seems likely that blocking of the parasympathetic outflow from the ganglion inhibits pain and autonomic symptoms that accompany various headache disorders. Yarnitsky et al have demonstrated that blocking the parasympathetic outflow from the SPG by intranasal application of lidocaine decreased head pain in migraine patients, but did not affect cutaneous allodynia.³² The authors suggested that blocking cranial parasympathetic outflow may decrease migraine pain by inhibiting the activation of peripheral intracranial nociceptors. It may be speculated that SPG blockade can modulate intracranial nociceptor activity in HC as well; however, this remains to be determined.

In this case, we used the Tx360[®] device for SPG blockade. This device has been shown as effective for this purpose in patients with chronic migraine.⁷ It should be noted that there are no studies comparing the efficacy of the different devices for SPG blockade in headaches. As for the selection of drug for SPG blockade, we used bupivacaine, as did Cady et al in their study on chronic migraine. However, this was an empiric decision to use bupivacaine as the optimal local anesthetic in this setting.

A possible pitfall to treatment using repeated SPG blocks, as used in this case, is that it requires patient cooperation and adherence to the scheduled protocol. Fortunately, our patient was fully compliant with her treatment plan, which resulted in decreased pain, improved functioning, mood and quality of life, as well as avoidance of emergency room visits or hospitalizations for headache treatment.

CONCLUSION

This clinical observation suggests that repetitive SPG blocks using local anesthetics may be an effective treatment for HC, specifically for patients who cannot tolerate indomethacin, or when this drug is contraindicated. While we did not observe an acute effect of SPG block on HC pain, repeti-

tive blocks over several weeks proved effective. Further studies are needed to prove efficacy of SPG block in HC.

STATEMENT OF AUTHORSHIP

Category 1

(a) Conception and Design

Michelle Androulakis

(b) Acquisition of Data

Michelle Androulakis

(c) Analysis and Interpretation of Data

Michelle Androulakis, Kaitlin Krebs, Avi Ashkenazi

Category 2

(a) Drafting the Manuscript

Michelle Androulakis, Kaitlin Krebs, Avi Ashkenazi

(b) Revising it for Intellectual Content

Michelle Androulakis, Kaitlin Krebs, Avi Ashkenazi

Category 3

(a) Final Approval of the Completed Manuscript

Michelle Androulakis, Kaitlin Krebs, Avi Ashkenazi

REFERENCES

1. The International Classification of Headache Disorders, 3rd edition (beta version). *Cephalalgia*. 2013;33:629-808.
2. Goadsby PJ. Trigeminal autonomic cephalalgias. *Continuum*. 2012;18:883-895.
3. Sjaastad O. Chronic paroxysmal hemicrania, hemicrania continua and SUNCT: The fate of the three first described cases. *J Headache Pain*. 2006;7:151-156.
4. Sluder G. *The Anatomical and Clinical Relations of the Sphenopalatine (Meckel's) Ganglion to the Nose and Its Accessory Sinuses*. AR Elliott Publishing Company; 1909.
5. Windsor RE, Jahnke S. Sphenopalatine ganglion blockade: A review and proposed modification of the transnasal technique. *Pain Physician*. 2004;7:283-286.
6. Cady R, Saper J, Dexter K, et al. A double-blind, placebo-controlled study of repetitive transnasal

- sphenopalatine ganglion blockade with tx360((R)) as acute treatment for chronic migraine. *Headache*. 2015;55:101-116.
7. Cady RK, Saper J, Dexter K, et al. Long-term efficacy of a double-blind, placebo-controlled, randomized study for repetitive sphenopalatine blockade with bupivacaine vs saline with the Tx360((R)) device for treatment of chronic migraine. *Headache*. 2015;55:529-542.
 8. Oluigbo CO, Makonnen G, Narouze S, et al. Sphenopalatine ganglion interventions: Technical aspects and application. *Prog Neurol Surg*. 2011;24:171-179.
 9. Piagkou M, Demesticha T, Skandalakis P, et al. Functional anatomy of the mandibular nerve: Consequences of nerve injury and entrapment. *Clin Anat*. 2011;24:143-150.
 10. Additional I, Candido KD, Masonic AI. A novel revision to the classical transnasal topical sphenopalatine ganglion block for the treatment of headache and facial pain. *Pain Physician*. 2013;16:E769-E778.
 11. Khan S, Schoenen J, Ashina M. Sphenopalatine ganglion neuromodulation in migraine: What is the rationale? *Cephalalgia*. 2014;34:382-391.
 12. Schoenen J, Jensen RH, Lanteri-Minet M, et al. Stimulation of the sphenopalatine ganglion (SPG) for cluster headache treatment. Pathway CH-1: A randomized, sham-controlled study. *Cephalalgia*. 2013;33:816-830.
 13. Seo JG, Park SP. Validation of the Patient Health Questionnaire-9 (PHQ-9) and PHQ-2 in patients with migraine. *J Headache Pain*. 2015;16:65.
 14. Shin HE, Park JW, Kim YI, et al. Headache Impact Test-6 (HIT-6) scores for migraine patients: Their relation to disability as measured from a headache diary. *J Clin Neurol (Seoul, Korea)*. 2008;4:158-163.
 15. Ashkenazi A, Levin M, Dodick D. Peripheral procedures: Nerve blocks, peripheral neurostimulation and botulinum toxin injections. In: Silberstein SD, Lipton RB, Dodick DW, eds. *Wolff's Headache Other Head Pain*, 8th ed. New York, NY: Oxford University Press; 2008:767-792.
 16. Robbins M, Robertson C, Kaplan E, et al. The sphenopalatine ganglion: Anatomy, pathophysiology, and therapeutic targeting in headache. *Headache*. 2015;56:240-258.
 17. Tepper SJ, Stillman MJ. Cluster headache: Potential options for medically refractory patients (when all else fails). *Headache*. 2013;53:1183-1190.
 18. Kittrelle JP, Grouse DS, Seybold ME. Cluster headache. Local anesthetic abortive agents. *Arch Neurol*. 1985;42:496-498.
 19. Robbins L. Intranasal lidocaine for cluster headache. *Headache*. 1995;35:83-84.
 20. Costa A, Pucci E, Antonaci F, et al. The effect of intranasal cocaine and lidocaine on nitroglycerin-induced attacks in cluster headache. *Cephalalgia*. 2000;20:85-91.
 21. Felisati G, Arnone F, Lozza P, et al. Sphenopalatine endoscopic ganglion block: A revision of a traditional technique for cluster headache. *Laryngoscope*. 2006;116:1447-1450.
 22. Pipolo C, Bussone G, Leone M, et al. Sphenopalatine endoscopic ganglion block in cluster headache: A reevaluation of the procedure after 5 years. *Neurol Sci*. 2010;31(Suppl 1):S197-S199.
 23. Schaffer JT, Hunter BR, Ball KM, et al. Noninvasive sphenopalatine ganglion block for acute headache in the emergency department: A randomized placebo-controlled trial. *Ann Emerg Med*. 2015;65:503-510.
 24. Pietzsch JB, Garner A, Gaul C, et al. Cost-effectiveness of stimulation of the sphenopalatine ganglion (SPG) for the treatment of chronic cluster headache: A model-based analysis based on the Pathway CH-1 study. *J Headache Pain*. 2015;16:530.
 25. Jurgens TP, Schoenen J, Rostgaard J, et al. Stimulation of the sphenopalatine ganglion in intractable cluster headache: Expert consensus on patient selection and standards of care. *Cephalalgia*. 2014;34:1100-1110.
 26. Puig CM, Driscoll CL, Kern EB. Sluder's sphenopalatine ganglion neuralgia--treatment with 88% phenol. *Am J Rhinol*. 1998;12:113-118.
 27. Narouze S, Kapural L, Casanova J, et al. Sphenopalatine ganglion radiofrequency ablation for the management of chronic cluster headache. *Headache*. 2009;49:571-577.
 28. Maizels M, Scott B, Cohen W, et al. Intranasal lidocaine for treatment of migraine: A randomized, double-blind, controlled trial. *JAMA*. 1996;276:319-321.
 29. Cohen S, Ramos D, Grubb W, et al. Sphenopalatine ganglion block: A safer alternative to epidural blood patch for postdural puncture headache. *Reg Anesth Pain Med*. 2014;39:563.