Noninvasive Vagus Nerve Stimulation and Electrotherapy for Headaches

Alexander Feoktistov

Essential Concepts

- Transcutaneous supraorbital nerve stimulation, noninvasive vagus nerve stimulation, and remote electrical neuromodulation devices provide noninvasive and nonpharmacological therapeutic options for patients with migraine and cluster headaches.
- These noninvasive neuromodulation devices could be safely used in office, at the bedside, or at home by patients.
- These clinically proven and drug-free methods of pain management should be utilized as additional treatment options for patients with migraine and cluster headaches.

1 Noninvasive Vagus Nerve Stimulation and Electrotherapy for Headaches

Overview

There are multiple classes of preventative and acute medications that are available to our patients with migraine and cluster headaches. Yet, as many as two-thirds of patients with migraine headaches, who are candidates for prophylactic therapy do not use them [1]. It has also been estimated that over 70% of patients discontinue preventative medication after 6 months of therapy. The most common reasons for that are lack of efficacy and side effects [2]. Clinically, we also encountered situations when drug interactions represent may pose a major concern. There are also

A. Feoktistov (✉)
Synergy Integrative Headache Center, Northfield, IL, USA
e-mail: drfeoktistov@synergyheadache.com

D. Souza et al. (eds.), *Bedside Pain Management Interventions*,
https://doi.org/10.1007/978-3-031-11188-4_28

patients who prefer nonpharmacological treatment modalities. With recent technological advances, we now have noninvasive and nonpharmacological treatment modalities that could be helpful in these situations.

Indications and Contraindications

All patients with migraine or cluster headaches (both chronic and episodic forms) require effective and reliable acute/abortive therapeutic options. All noninvasive neuromodulation devices can be safely utilized in conjunction with more traditional pharmacological interventions. In general, we recommend use of neuromodulation devices in patients with contraindications to triptans and ergotamine-containing medications, in patients who experience side effects from their current acute or prophylactic therapy, or in those who are unsatisfied with therapeutic outcomes. Another group of patients that may benefit from nonpharmacological acute or prophylactic treatment options are patients with medication overuse headache or patients with an acute medication overuse who are at risk of developing medication overuse headache. Also considering the remarkable safety profile of these neuromodulation devices it is hard to find a patient who may not benefit from at least a trial of such therapeutic intervention. That being said, it is important to recognize that these devices have not been studied and therefore safety and efficacy have not been established in the pediatric population, adolescents or pregnant/nursing patients.

Clinical Anatomy

The vagus nerve (tenth cranial nerve) is the largest cranial nerve and it contains both afferent and efferent fibers. It enters the central nervous system via the trigeminal nuclear caudalis in the brainstem and proceeds further into the periaqueductal gray and raphe nucleus [3]. In the neck area, the vagus nerve travels within the sheath of the carotid artery and can be found at an average depth of 1.3–1.5 cm in the anterior cervical triangle (where we would normally palpate carotid pulse) [4]. Stimulation of the vagus nerve has been shown to reduce central excitability via the reduction of glutamate in the trigeminal nucleus caudalis, suppression of spontaneous neuronal firing in the trigeminal cervical complex, as well as suppression of cortical spreading depression susceptibility [5, 6].

The trigeminal nerve is the main sensory nerve in the head and face. Its anatomy has been well described. It appears that external trigeminal nerve stimulation reduces hypometabolism in the areas of the brain involved in central pain control (orbitofrontal and rostral anterior cingulate areas) [7].

Nonpainful remote electrical stimulation that is applied to the distant from the headache area (upper arm) has been shown to activate the descending antinociceptive pathway via the conditioned pain modulation effect [8].

Equipment and Supplies

All neuromodulation techniques described here are noninvasive and require no anesthesia or guidance. Noninvasive vagus nerve stimulation requires a hand-held stimulator marketed under the name GammaCore (Fig. 1). The GammaCore device, depending on the stimulation pattern, can be utilized as an acute therapeutic option for migraine treatment and/or as an acute or prophylactic option for cluster headache treatment.

An external trigeminal nerve stimulator, marketed under brand name Cefaly, can also be utilized as an acute or preventative migraine therapy. Currently, there is a single Cefaly device available that provides both acute and prophylactic stimulation.

Finally, the remote electrical stimulation device marketed under the brand name Nerivio is approved for acute treatment of migraine headaches and is controlled via smartphone app (Fig. 2).

Stimulation Technique and Protocol

When using noninvasive vagus nerve stimulation, the patient should be instructed to palpate the carotid pulse on the anterolateral area of the neck (which represents the correct treatment/stimulation location) at the earliest sign of pain. The patient should then apply a small amount of supplied gel to the stimulation surface of the device, turn the device on, and position it vertically along the pathway of the vagus nerve/carotid artery. Stimulation should be adjusted gradually by the patient until he/she experiences a slight pull or twitching at the corner of the lip. This muscular

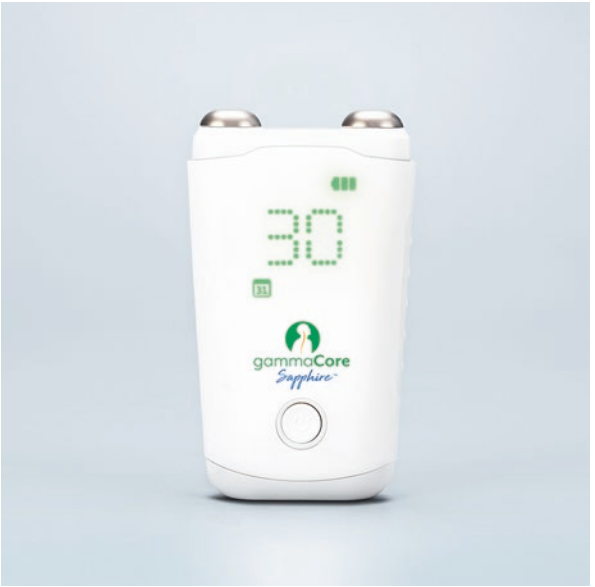

Fig. 1 Noninvasive vagus nerve stimulator. Noninvasive vagus nerve stimulation provides safe, effective and easy to use treatment of migraine headache. This particular treatment modality offers both acute and prophylactic stimulations. Image reprinted with permission from ElectroCure

Fig. 2 Remote electrical stimulation device. Remote electrical stimulation device provides novel noninvasive acute therapy for patients with migraine headache. The stimulation is applied as needed and should be initiated at migraine onset. The stimulation should be perceived by the patient as strong (but not painful) and last for 45 min. (Image - courtesy of Dmitri Souza MD, PhD)

activation signals that the intensity of the stimulation is significant enough to capture vagus nerve fibers.

If this stimulation is used to treat a migraine headache the patient should administer two 2 min stimulations at the earliest sign of migraine pain. If the patient continues to experience pain 20 min after the start of the first treatment, the patient may

administer 2 more stimulations. The patient may administer the third additional treatment (consisting of two 2 min stimulations) if pain persists 2 h after the start of treatment 1 [9].

If noninvasive vagus nerve stimulation is being used to acutely treat episodic cluster headache the patient should administer treatment consisting of three 2 min stimulations at the onset of the cluster headache attack. If pain persists, the patient may administer the second treatment (consisting of three 2 min stimulations) 3 min after completion of the first treatment. The patient may treat up to 4 attacks for a total of 24 stimulations per day [10–12].

For cluster headache prophylaxis the patient should administer the first treatment (consisting of three 2 min stimulations) within 1 h of waking. A second treatment should be administered at least 7–10 h after the first treatment.

When using external trigeminal nerve stimulation (Cefaly) as an acute treatment for migraine headache, patients should apply an adhesive electrode to the lower frontal area (between eyebrows) at the onset of a migraine attack. Next the patient should attach the stimulator to the electrode and activate the stimulator by pressing the button and administer 1-hour of high-frequency stimulation. If the stimulator is used prophylactically, the patient should apply the adhesive electrode and stimulator in a similar way and activate preventive stimulation consisting of a 20-minute low-frequency session.

When using a remote electrical stimulation device (Nerivio) advise patients to initiate stimulation within 60 min of migraine onset. The patient should apply the device to the upper arm and secure it with the supplied supporting armband. Using a smartphone app, the patient should gradually increase treatment intensity to the level that feels strong, yet not painful. Treatment should continue for 45 min [8].

Potential Complications and Adverse Events

Overall, all noninvasive neuromodulation treatment modalities have been found to be safe and well-tolerated. The most common device-related adverse events with noninvasive vagus nerve stimulation were application site erythema and discomfort and perioral myokymia during treatment.

The most common side effects noticed with external trigeminal nerve stimulations were intolerance to the paresthesia in the forehead, sensation of fatigue/sedation during and shortly after the treatment, and headache.

The most common adverse reactions related to remote electrical neuromodulation devices were muscle spasms, arm pain, a sensation of warmth and/or numbness at the application site, and redness.

Clinical and Technical Pearls

- When using noninvasive vagus nerve stimulation patients should apply the conductive gel before each stimulation.

- Noninvasive vagus nerve stimulation could be administered on the same side of the neck or the patient may switch sides if desired.
- Inform the patient of the risk of uncomfortable paresthesias in the distribution of the supraorbital and supratrochlear nerves during external trigeminal nerve stimulation.
- Advise patients that external trigeminal nerve stimulation should be applied daily for at least 2 months to achieve a consistent reduction in migraine frequency.
- Advise patients to initiate remote electrical neuromodulation treatment within 60 min from the migraine onset.

References

1. Lipton RB, Bigal ME, Diamond M, Freitag F, Reed ML, Stewart WF. Migraine prevalence, disease burden, and the need for preventive therapy. Neurology. 2007;68(5):343–9.
2. Hepp Z, Dodick DW, Varon SF, Gillard P, Hansen RN, Devine EB. Adherence to oral migraine-preventive medications among patients with chronic migraine. Cephalalgia. 2015;35(6):478–88.
3. Yuan H, Silberstein SD. Vagus nerve and vagus nerve stimulation, a comprehensive review: part i. Headache. 2016;56(1):71–8.
4. Frangos E, Komisaruk BR. Access to vagal projections via cutaneous electrical stimulation of the neck: fMRI evidence in healthy humans. Brain Stimul. 2017;10(1):19–27. https://doi.org/10.1016/j.brs.2016.10.008.
5. Akerman S, Simon B, Romero-Reyes M. Vagus nerve stimulation suppresses acute noxious activation of trigeminocervical neurons in animal models of primary headache. Neurobiol Dis. 2017;102:96–104. https://doi.org/10.1016/j.nbd.2017.03.004.
6. Nonis R, D'Ostilio K, Schoenen J, Magis D. Evidence of activation of vagal afferents by non-invasive vagus nerve stimulation: an electrophysiological study in healthy volunteers. Cephalalgia. 2017;37(13):1285–93.
7. Magis D, D'Ostilio K, Thibaut A, De Pasqua V, Gerard P, Hustinx R, et al. Cerebral metabolism before and after external trigeminal nerve stimulation in episodic migraine. Cephalalgia. 2017;37(9):881–91.
8. Yarnitsky D, Dodick DW, Grosberg BM, Burstein R, Ironi A, Harris D, et al. Remote electrical neuromodulation (REN) relieves acute migraine: a randomized, double-blind, placebo-controlled, multicenter trial. Headache. 2019;59(8):1240–52. https://doi.org/10.1111/head.13551.
9. Yarnitsky D, Volokh L, Ironi A, Weller B, Shor M, Shifrin A, et al. Nonpainful remote electrical stimulation alleviates episodic migraine pain. Neurology. 2017;88(13):1250–5. https://doi.org/10.1212/WNL.0000000000003760.
10. Silberstein SD, Mechtler LL, Kudrow DB, Calhoun AH, McClure C, Saper JR, et al. Non–invasive vagus nerve stimulation for the ACute treatment of cluster headache: findings from the randomized, double-blind, sham-controlled ACT1 Study. Headache. 2016;56(8):1317–32.
11. De Coo IF, Marin J, Silberstein SD, Friedman DI, Gaul C, Tyagi A, et al. Non-invasive vagus nerve stimulation for acute treatment of episodic and chronic cluster headache: pooled analysis of data from two randomized, double-blind, sham-controlled clinical trials. Cephalalgia. Conference: 18th congress of the international headache society, IHC 2017. Canada, 2017;37(1 Supplement 1):175–176. https://www.cochranelibrary.com/central/doi/10.1002/central/CN-01470041/full
12. Goadsby PJ, de Coo IF, Silver N, Tyagi A, Ahmed F, Gaul C, et al. Non-invasive vagus nerve stimulation for the acute treatment of episodic and chronic cluster headache: a randomized, double-blind, sham-controlled ACT2 study. Cephalalgia. 2018;38(5):959–69.

Further Reading

Diener HC, Goadsby PJ, Ashina M, et al. Non-invasive vagus nerve stimulation (nVNS) for the preventive treatment of episodic migraine: the multicentre, double-blind, randomised, sham-controlled PREMIUM trial. Cephalalgia. 2019;39(12):1475–87.

Evers S. Non-invasive neurostimulation methods for acute and preventive migraine treatment-A narrative review. J Clin Med. 2021;10(15):3302.