

GAMMACORE DEVICE FOR CHRONIC POSTTRAUMATIC HEADACHE PAIN MANAGEMENT IN VETERANS WITH COMORBID MOOD DISORDERS: A CASE REPORT

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Background: Chronic posttraumatic headache (CPTH) is a prevalent condition following traumatic brain injury, especially among veterans, with a significant impact on quality of life. Traditional treatments often lack efficacy and evidence-based support.

Case Report: We report the case of a 46-year-old male veteran with CPTH, nonresponsive to standard therapies, including botulinum toxin A and oral medications. The patient underwent treatment with the gammaCore vagus nerve stimulator, a US Food and Drug Administration-cleared device intended for migraine and cluster headache management.

Conclusions: Following initiation of gammaCore therapy, the patient experienced a marked reduction in headache intensity and frequency, alongside significant improvements in anxiety levels. These outcomes suggest that gammaCore may be a promising noninvasive treatment option for CPTH, particularly in patients with coexisting mood disorders. Further research is warranted to validate these findings and establish gammaCore's role in CPTH management.

Key words: gammaCore, chronic posttraumatic headache, CPTH, veterans, case report

BACKGROUND

Head pain, also known as cephalalgia, is the most prevalent physical complaint following traumatic brain injury (TBI), with prevalence rates ranging from 10% to 90%. Among these patients, 18% to 22% report experiencing posttraumatic headaches one year after the injury. Chronic posttraumatic headache (CPTH) is defined as a secondary headache that arises within 7 days following head trauma or after regaining consciousness. Headaches are the most common type of chronic pain after TBI, particularly CPTH, which has a prevalence of 47% to 95% in mild TBI cases, compared to 20% to 38% in moderate-to-severe TBI (1). Literature indicates that the incidence of CPTH is 44%, with a cumulative incidence of 71% at 12 months, including a 20% rate of new headaches occurring between

3-12 months postinjury (2). For military personnel, the incidence of CPTH is reported to be 16% to 27% at 3 months and 20% to 28% at 12 months, according to a large US military study (3). Clinically, CPTH often resembles primary headache types, including migraines and tension-type headaches. Potential mechanisms contributing to CPTH pain include both peripheral and central causes. Regarding peripheral origins, TBI can result in the sensitization of nociceptors both intracranially and extracranially. Intracranial sensitization occurs due to neurogenic inflammation, which leads to hypersensitivity of cranial nociceptors. Extracranially, peripheral tissues, such as bone, muscle, and ligaments, innervated by pain receptors associated with A-delta and C fibers, may also become sensitized. Additionally, damage to cranial nerves from direct mechanical injury

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or vascular trauma can lower the activation threshold, resulting in hyperstimulation and an increased response to noxious stimuli, particularly within the trigeminal sensory system. On the central side, CPTHAs may stem from damage to spinothalamic and thalamocortical pathways, altering the central control over nociceptive input (1). Hyperadrenergic activity, resulting from disturbances in cortical neurons, is another factor contributing to the development of CPTHAs.

Current treatment options are based on primary headache pain disorders as CPTHAs often present as migraine, tension, cervicogenic, or cluster-type headaches. For instance, migraine-like phenotype of CPTHAs is treated with oral medication, including triptans and nonsteroidal anti-inflammatory drugs (NSAIDs) for acute management and topiramate or tricyclic antidepressants for preventative management, while botulinum toxin injections can be resorted to as an interventional option. Nevertheless, there is a lack of quality literature supporting the efficacy and evidenced-based use of any acute and preventive pharmacological treatment for CPTHAs (4).

This case report presents an alternative and effective noninvasive treatment for CPTHAs in veterans with comorbid mood disorders, utilizing the gammaCore™ vagus nerve stimulator (ElectroCore, Inc, Rockaway, NJ). This US Food and Drug Administration (FDA)-cleared device is indicated for the acute and preventive treatment of migraine and cluster headaches. Our follow-up data, including pain scores (Visual Analog Scale [VAS]) and anxiety levels before and after treatment, demonstrates the high clinical efficacy of the device in managing CPTHAs in veterans with concurrent mood disorders. Given the existing literature and qualitative data supporting the use of the gammaCore device for migraine treatment, along with the overlap between current CPTHAs treatment protocols and migraine management, the positive outcomes observed in this case warrant further prospective studies to validate the use of the gammaCore device for treating CPTHAs.

We present the case of a 46-year-old male veteran patient with CPTHAs with unremitting headaches refractory to oral medication and botulinum toxin A injection started on the gammaCore vagus nerve stimulator therapy as a possible treatment option to alleviate CPTHAs pain. Informed consent of the patient was taken and the study included anonymous clinical data of the patient. No Institutional Review Board approval was

required as per medical center policy for conducting a case report.

CASE PRESENTATION

Patient Description

A 46-year-old male veteran with a history of post-traumatic stress disorder (PTSD), anxiety disorder, TBI, obstructive sleep apnea, and conductive hearing loss.

Case History

The patient sustained a TBI, in 2006, in Iraq due to an improvised explosive device blast while driving, resulting in symptoms of dizziness, headaches, and tinnitus, without loss of consciousness. He reported headaches occurring 3-4 times a week, characterized as throbbing and sharp, with intensity ranging from 6/10 to 8/10 VAS score and lasting up to 7 hours. The headaches were accompanied by light and noise sensitivity, cognitive difficulties, and worsening mood symptoms, including anxiety and depression, as well as insomnia. Previous treatments, including ibuprofen, Excedrin, Tylenol, acupuncture, physical therapy, and chiropractic care, yielded minimal relief.

Physical Examination Results

The examination revealed anxiety and cognitive impairment. Tenderness in the occipital region was noted, and neurological assessments showed no focal deficits.

Results of Pathological Tests and Other Investigations

Cervical spine x-rays and imaging studies showed no remarkable findings. The patient was taking Maxalt (10 mg as needed) and topiramate (50 mg nightly) for headache management.

Treatment Plan

The initial treatment involved administering 190 units of botulinum toxin A for CPTHAs. After limited improvement, bilateral occipital nerve blocks were attempted. The patient then trialed the gammaCore vagus nerve stimulator.

Expected Outcome of the Treatment Plan

The expected outcome was a reduction in headache frequency and intensity, as well as improvements in associated anxiety symptoms.

Actual Outcome

During the 3-month follow-up, the patient was

assessed for continuous device adherence and any reported adverse effects using a self-reported questionnaire. He stated complete adherence to therapy during acute attacks and preventative treatment with no side effects. The patient reported that his CPTHAs were “pretty controlled,” with headache intensity decreasing from an average of 6/10 to 3/10 (VAS score) and frequency reducing to 1-2 times per week. He also noted a significant improvement in anxiety levels, indicating the efficacy of the gammaCore device as part of his treatment plan. The gammaCore device is approved to be used for acute attacks and prevention of headaches in the setting of migraines, and the same protocol was taken for management of CPTHAs. As per protocol, for preventative treatment, the gammaCore device was used twice daily. This involves two 2-minute stimulations on the same side of the neck, both in the morning and at night. For attacks, the device is used when symptoms arise, performing two 2-minute stimulations on the same side of the neck and repeating if the pain persists.

DISCUSSION

The incidence of CPTHAs among veterans and combat soldiers can reach as high as 28% within 12 months, underscoring the need for evidence-based treatment options. The gammaCore device, which is FDA-cleared, is indicated for the acute and preventative treatment of migraine and cluster headaches through vagus nerve stimulation. Current treatments for CPTHAs are largely derived from those for primary headache disorders, as CPTHAs frequently resemble migraine-type headaches. The standard approach involves the use of NSAIDs or triptans for acute management and antiepileptics or tricyclic antidepressants for prevention, paralleling migraine treatment strategies. However, there is a notable lack of robust literature supporting the efficacy of pharmacological treatments for CPTHAs (4).

Further applying migraine treatment methods to CPTHAs can be seen with the use of the gammaCore device, originally approved for migraine and cluster headache management. In our case, the patient experienced a 50% reduction in VAS scores (from 6/10 to 3/10) along with significant improvements in anxiety. This suggests that the device’s mechanism of action—stimulating the vagus nerve—may contribute to its effectiveness. Notably, the gammaCore offers a compelling alternative due to its high clinical efficacy and favorable safety profile, as its common side effects occur in only up to 2% of

users (including localized discomfort, muscle twitching, headache, dizziness, and tingling).

The gammaCore device is distinctive in that it simultaneously addresses both pain and anxiety. Chronic pain and anxiety often exist in a cyclical relationship, significantly influencing each other. This can be largely attributed to the higher-level connections in the amygdala as it is an important brain center for the emotional-affective dimension of pain and for pain modulation. Hyperactivity in the central nucleus of the amygdala, also known as the “nociceptive amygdala,” accounts for pain-related emotional responses and anxiety-like behavior. Abnormally enhanced output from the central nucleus is the consequence of an imbalance between excitatory and inhibitory mechanisms. Impaired inhibitory control mediated by a cluster of gamma-aminobutyric acidergic interneurons in the intercalated cell masses allows the development of glutamate and neuropeptide-driven synaptic plasticity of excitatory inputs from the brain stem. Increased amygdala output as the result of neuroplasticity in the central nucleus has emerged as an important contributor to emotional-affective behaviors in animal pain models (5). This strong connection highlights the importance of treating both physical and emotional symptoms. Importantly, our focus is on veterans and combat soldiers, who exhibit a higher prevalence of comorbid PTSD compared to the general population with CPTHAs. Notably, anxiety disorders frequently co-occur with PTSD in this demographic, with 73.3% of veterans diagnosed with PTSD also experiencing another anxiety disorder, 39.3% of which is generalized anxiety disorder (6).

Research indicates that PTSD adversely affects the disability levels of chronic pain patients, including those with CPTHAs. Patients suffering from headache pain and PTSD tend to experience significantly greater disability than those without PTSD (7). Therefore, it is encouraging that addressing concurrent mood disorders, particularly PTSD and anxiety, may lead to more effective clinical outcomes when managed alongside CPTHAs. The gammaCore device provides a noninvasive solution that targets pain, while also alleviating mood disorders through vagus nerve stimulation.

Limitations

Limitations of this study include the reliance on subjective diagnostic methods, with no objective measures, such as tests or imaging to support the findings. The subjective nature of self-reported outcomes and clinical

cian observations may further impact the validity of the results. As a case report, the study's findings have limited generalizability, and the absence of a control group restricts the ability to draw definitive conclusions regarding the effectiveness or safety of the gammaCore intervention.

CONCLUSIONS

Given the absence of a first-line therapy or scientifically validated treatment specifically for CPTH, and considering that headache pain is the most prevalent

pain generator following TBI, with significant disability rates in veterans, the use of the gammaCore device at Veterans Affairs Medical Centers, where there is a high population of veterans, represents a valuable intervention worth exploring. This is particularly relevant for patients dealing with concurrent mood disorders like PTSD and generalized anxiety disorder. Further prospective studies, including case series and randomized controlled trials with a larger sample size and control group, are needed to evaluate the efficacy of the gammaCore device in the treatment of CPTH.

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