Efficacy of Stellate Ganglion Block in the Treatment of Anxiety Symptoms From Combat-Related Post-Traumatic Stress Disorder: A Case Series

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ABSTRACT Objective: Report the efficacious use of stellate ganglion blocks (SGBs) in treating the anxiety symptoms of four patients diagnosed with combat-related post-traumatic stress disorder (PTSD) and discuss possible mechanisms of action to explain these findings. Background: Successful treatment of PTSD with SGB has been demonstrated and reported previously at Walter Reed Army Medical Center. An identical protocol was used at Tripler Army Medical Center to treat four service members diagnosed with combat-related PTSD. Methods: All patients reported received an SGB on the right side at the level of C6. The patient's PTSD symptoms were evaluated using the Post-traumatic Stress Disorder Checklist (PCL). This checklist was distributed one day before treatment and again the day following treatment. The patients were also given the PCL at subsequent follow-up visits to quantify sustained benefit. Results: SGB showed acute benefit for the symptoms of PTSD by markedly reduced PCL scores after the procedure. Benefits were also sustained during close outpatient follow-up. Conclusion: Selective blockade of the right stellate ganglion at C6 is a minimally invasive procedure with an excellent safety profile that may provide sustained relief of PTSD symptoms. The procedure may also provide benefit for those who are resistant to psychotropic intervention.

INTRODUCTION

Post-traumatic stress disorder (PTSD) is a pathological symptomatology that can develop in certain individuals following exposure to an overwhelmingly traumatic event. The symptomatology includes patients reexperiencing the events of the trauma often through intense, intrusive, and vivid memories. Nightmares are common and often involve elements from the individual's memory of the trauma. Patients may also experience waking recollections of the trauma commonly called "flashbacks." During these recollections, the individual will act as if the original trauma is actually going on around them and may, in extreme cases, have perceptual disturbances including visual and/or auditory hallucinations. Other symptoms of the disease include avoidance of stimuli that may remind them of the trauma including activities, places, or people. They also may exhibit a general numbing of responsiveness marked by diminished interest in activities and general detachment from others. Along with detachment, individuals have symptoms of increased arousal as indicated by difficulty with sleep, increased irritability, problems in concentrating, and exaggerated startle response.[1,2]

The underlying etiology of PTSD appears to be heavily influenced by one's autonomic susceptibility. Individuals diagnosed with PTSD have shown increased catecholamine levels, namely norepinephrine, in both cerebrospinal fluid and 24-hour urine levels.[3,4] Further evidence for sympathetic involvement was shown when patients' symptoms worsened with the administration of yohimbine, a noradrenergic agonist.[5] The hypothalamic–pituitary–adrenal axis also documented increased levels of corticotrophin-releasing hormone in cerebrospinal fluid, which is similar that seen in major depressive disorder.[6] However, unlike individuals with depression, cortisol levels are not resistant to suppression with the administration of dexamethasone.[7] Given the fact that corticotrophin-releasing hormone is stimulated by both glucocorticoids and catecholamines, this effect further supports the conclusion that the sympathetic system plays a strong role in the etiology of PTSD.

The prevalence of PTSD in military personnel has been rising steadily over the past decade. The reason for this is likely multifactorial with the ongoing psychiatric toll of combat trauma and recurring deployment cycles. Some of the most recent data collected by the Department of Defense survey showed that PTSD incidence rose from 7% to 11% (from 2005 to 2008). Along with increases in PTSD, attempted suicide rates doubled from 1% to 2%.[8] Studies have shown an increased risk of suicide in those diagnosed with PTSD.[9] Given this fact, it is becoming increasingly important that more efficacious treatment modalities be used.

Recent medical treatment for PTSD has relied heavily on pharmacologic modalities. Conventional first-line treatments include selective serotonin reuptake inhibitors (SSRIs), selective norepinephrine reuptake inhibitors (SNRIs), and mirtazapine. These medications work by increasing the serotonin/norepinephrine available in the synaptic cleft and thereby, over the course of several weeks, changing the concentration of postsynaptic receptors. Although the safety and side-effect profiles of these medications are relatively benign, the response rate, discontinuation rate, and overall efficacy leave much to be desired.

SSRIs, despite the relatively low side-effect profile, have a high discontinuation rate ranging from 30% to 50%.[10] All of

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these medications take anywhere from 4 to 8 weeks to take effect, which places individuals at increased risk of suicide during this latency period. The overall efficacy of these modalities have also proven to be moderate at best with a symptom rate of response averaging around 60%.[11–13] Some research has indicated improvement with risperidone or olanzapine as augmentation agents with failed response to high-dose SSRI/SNRI.[14,15] However, these medications also increase side effects including risks of extrapyramidal symptoms, metabolic abnormalities, and possible tardive dyskinesia with long-term use. Given these limitations, alternative treatment modalities targeting the sympathetic nervous system have developed in recent years.

Recent research has shown that the alpha-1 antagonist, prazosin is effective at reducing nightmares commonly seen in PTSD.[16] Along with its effectiveness during sleep, there has been some suggestive work that it may also be beneficial when dosed during the day.[17] Other successful treatments targeting the sympathetic nervous system include endoscopic sympathetic block and stellate ganglion block (SGB). Both of these treatments have reported improvement of anxiety symptoms; however, endoscopic sympathetic block is significantly more invasive, associated with more side effects, and is irreversible. A prior case series published in 2010 showed effective treatment of combat-related PTSD with SGB. The goal of this article is to advance the published data pertaining to PTSD successfully and safely treated with SGB. We will discuss four cases where individuals diagnosed with PTSD were able to obtain sustained benefit with SGB as well as minimal side effects. All of these patients failed several psychopharmacologic interventions and several even required prior hospitalization for their psychiatric symptoms. After the procedure, all of these individuals were able to return to some form of duty and also slowly titrated off many of their psychotropics.

METHODS

Patient was given information concerning the risk/benefits of the procedure and a consent form was completed. An intravenous line was started with a 22G IV in the left hand. The patient was positioned comfortably in the supine position and prepped and draped in the sterile fashion. Radiographic confirmation of the right C6 transverse process was obtained using c-arm X ray. For patient comfort, the skin was anesthetized with 1 cc of 2% lidocaine. Using an anterior paratracheal approach, a 25-gauge Quincke needle was passed under fluoroscopic guidance until it contacted the transverse process of the C6 vertebra and then was pulled back 1 mm. Appropriate needle position was then confirmed by injection of 2 cc of iohexol (180 mg/mL) radio-opaque dye to monitor its spread. After negative aspiration, 7 cc of 0.5% ropivacaine was slowly injected to produce a sympathetic block. We monitored the patient's right hand temperature for 15 minutes following the anesthetic administration to confirm successful blockade of the cervical sympathetic ganglia as evidenced by an increase of at least 1.5°C. We also observed the patient for facial anhidrosis and Horner's syndrome symptoms (namely ptosis and miosis) for further confirmation.

PSYCHOMETRIC TESTING

The Post-traumatic Stress Disorder Checklist (PCL) is a 17-item psychometric test commonly used to screen, diagnose, and monitor symptom changes in individuals suspected/diagnosed with PTSD. A total symptom severity score (range 17–85) can be obtained by summing the scores from each of the 17 items. It was developed based on the symptoms criteria for PTSD from the Diagnostic and Statistical Manual of Mental Disorders.[1] There are three versions of the test: M (military), C (civilian), and S (specific). Given that our patients were all active duty military members with combat-induced symptoms, we used the M version for monitoring. Different cut-off scores have been suggested for both screening and diagnosis. One study of active duty members returning from combat recommended that a score of 28 was sensitive for the diagnosis of PTSD.[18] Other studies have recommended a score of 50 to optimize both sensitivity and specificity.[19] All patients included in this study had scores >50 before the procedure and were already diagnosed with PTSD.

CASE REPORTS

Case 1

The patient was a 34-year-old male with two deployments to Iraq from 2006 to 2007 and 2009 to 2010 as a combat medic. He was exposed to combat trauma during both deployments witnessing several members of his unit killed with improvised explosive devices and having to recover the bodies. The patient's PTSD symptoms started during his first deployment taking the form of reexperiencing through nightmares (approximately 3 per week) and recurrent intrusive thoughts, avoidance of crowded areas, and increased arousal in the form of difficulty falling and staying asleep (2–3 hours per night), outbursts of anger, hypervigilance, and exaggerated startle response (started after second deployment, patient's children started startling him on purpose for fun until he broke his son's arm). Interventions by his mental health providers included trials of citalopram, buspirone, Prozac, Wellbutrin, Minipress and sertraline, and individual therapy. All of these treatments were unsuccessful at controlling his symptoms.

Approximately 4 months after his second deployment, in the context of marital discord stemming from his PTSD symptoms, the patient attempted to kill himself by cutting his wrists in a hot bath. He was found by his wife, brought tothe Tripler Army Medical Center (TAMC) Emergency Department and eventually admitted to inpatient psychiatry. During his inpatient stay, patient was referred for SGB. PCL-M was administered immediately before the block and recorded at 64. PCL-M was then readministered 72 hours after the procedure and had decreased to 22. The patient and family noticed immediate improvement and reduction in symptoms. His PCL-M administered one month later was 35 and opted for a second SGB. His PCL-M measured 2 weeks after the second procedure was 29 with subjective improvement in his symptoms. The patient's records reviewed 3 months after

the second procedure indicated continued sustained benefit with minimal anxiety symptoms that were being successfully controlled with low-dose Celexa and buspirone.

Case 2

The patient was a 35-year-old male with 8 years time in service (Army) as a truck driver. He had two deployments to Iraq from 2004 to 2005 and 2007 to 2008. The patient also had significant history of childhood physical abuse. He was diagnosed with PTSD before entering the military related to an incident where he was beaten severely by his father with a large plank at the age of 12. The patient started drinking as a teenager and had a history of ethyl alcohol (ETOH) dependence. During his first deployment to Iraq, the patient was involved in 4 separate convoys hit by improvised explosive devices and was involved in 8 firefights. During this time the patient also reports psychological disturbance from seeing burning/dismembered bodies. He initially screened 41 out of 85 on his as PCL-C on March 16, 2009. He was admitted to the inpatient psychiatric ward 4 times between March 22, 2009 and November 15, 2010 for suicidality in the context of ETOH intoxication and PTSD symptoms. Stays were between 3 and 37 days with one discharge to a dual diagnosis program for 6 weeks. The patient's PCL-C score measured on December 31, 2009 was 85 out of 85. During this time, the patient had been in close contact with behavioral health and was attending PTSD groups. The patient had been tried on the following psychotropics with little improvement during the course of his treatment: trazodone, Remeron, Celexa, Zoloft, risperidone, naltrexone (ETOH), disulfiram (ETOH), and lithium.

During the patient's final say on the TAMC psychiatric inpatient ward, he scored 80 or 85 on his PCL-M. He was referred to anesthesiology for SGB on November 16, 2010. Two days after the procedure, he was discharged from the ward, his PCL-M having dropped to 18, and his suicidal ideation having completely resolved. The patient was unfortunately lost to follow-up after discharge.

Case 3

The patient was a 46-year-old male with one deployment to Iraq (2008–2009). During his deployment he was hiding in a shack during a mortar attack. One of the mortars landed a few feet from the shack causing direct injury to the patient and others in his squad. Throughout the deployment, he was attacked by small arms fire requiring the patient to take cover and return fire. The patient admitted that during these times he experienced extreme fear and helplessness.

After returning from deployment, he was diagnosed with PTSD. His symptoms included mood swings; insomnia with recurrent nightmares, reliving the events; intense psychological and physiological reactivity when exposed to internal and external cues with exaggerated startle response; efforts to avoid thoughts, feelings and conversations, feeling detached and estranged from others, restricted range of affect; outbursts of anger, avoidance of crowds, crying spells; and generalized hypervigilance. Following deployment, the patient did not develop substance abuse, but did experience relational problems with his wife. He initially underwent a course of cognitive behavior therapy and prolonged exposure therapy for his symptoms, but was only minimally responsive to both. During his treatment he was tried on sertraline, bupropion, Paxil, Ativan, and clonazepam for anxiety and depressive symptoms as well as trazodone for sleep. All of these psychotropics proved ineffective at controlling his PTSD symptoms.

At the time of SGB the patient's PCL-M score was 69. He experienced significant relief of symptoms after the procedure though he had a cough for 3 to 4 hours afterward and only a partial Horner's syndrome. At one month follow-up, he acknowledged sustained benefit with a PCL-M of 34.

Case 4

The patient was a 29-year-old male with one deployment to Iraq from 2008 to 2009. While in Iraq, the patient was exposed to several firefights and was one of the primary members involved in casualty cleanup. During this time, he was exposed to dismembered bodies including several friends in his unit. On returning home in September 2009, the patient noticed that he started to increase his alcohol intake eventually becoming dependent. He went through outpatient substance abuse treatment, however, continued to drink in lesser amounts.

Shortly after his substance abuse treatment, he was seen by outpatient psychiatry for continued aggressive behavior and insomnia. He was started on medications including Zoloft and Ambien with little improvement in his symptoms. The patient admitted that during this time he had difficulty sleeping because of frequent nightmares and would often awaken with substantial diaphoresis. He also expressed avoidance symptoms including fear of crowds, diminished interest in previously pleasurable activities, and general detachment from others including his family and friends. He acknowledged increased startle response and frequent anger outburst. His symptoms continued until he self-presented to the outpatient clinic at TAMC complaining of homicidal ideation toward several members of his chain of command. He was subsequently admitted to the active duty inpatient ward and officially given the diagnosis of PTSD.

While on the ward, he displayed a general adversity to any medications and would become enraged at the thought of starting further medication. The patient was offered the option of receiving an SGB. He consented to the procedure and was given the PCL-M 3 days before the procedure. His initial PCL-M score was 76. He received the procedure with no prominent side effects. The patient acknowledged immediate improvement in his hyperarousal symptoms. The next day his PCL-M was readministered and the patient scored a 24.

DISCUSSION

SGB is a relatively noninvasive procedure with few side effects that has been in use since the 1920s for the treatment of pain (migraines, herpes zoster, and sympathetic mediated pain to include complex regional pain syndrome). Recently,

SGB has been used at Walter Reed Army Medical Center and TAMC for treatment of refractory PTSD. Although this case series shows efficacy of this treatment for some patients, it raises more questions than it answers.

First, the mechanism of action has yet to be elucidated. Although Maihöfner et al[20] demonstrated activation of insular cortex during mechanical hyperesthesia (pain with light touch) with complex regional pain syndrome and Liberzon and Martis[21] demonstrated insular cortex activation in PTSD patients, the mechanism of activation remains unclear for both conditions and insular deactivation remains to be shown in patients treated with SGB. Suggestions that the connection between the stellate ganglion and the hypothalamus is responsible for the changes based on Westerhaus and Loewy demonstration of connection are without foundation as they utilized a pseudorabies virus to show this connection (pseudorabies being a reverse axonal virus showing input from hypothalamus to stellate ganglion and not vise versa).[22] Lipov et al[23] hypothesize that after SGB the resulting decrease in nerve growth factor leads to reduction in norepinephrine, and deactivation of intracerebral pathologic states shows the most promise at this point; however, the mechanism needs further elucidation and biochemical verification in patients treated specifically for PTSD.

More important than actual mechanism, however, are quantification of efficacy on a population level, comparison of efficacy to other treatments, better defining the duration of symptom relief, and discovering whether results separate from sham procedure. Given the dramatic results seen in this case series as well as the case series by Mulvaney et al,[24] future studies into these variables are of paramount importance in defining the role of SGB in the treatment of PTSD.

CONCLUSION

As found in prior case studies, SGB appears to be not only safe but also efficacious in the treatment of PTSD symptoms. Given that none of the patients presented in this case series were psychotropic naive and indeed several were totally resistant, further weight can be given to the possibility that SGB may prove to be beneficial for medication of nonresponders. Although the mechanism of action for the procedure's efficacy remains unknown, the objective findings seem to argue the case of long-term neuronal changes. Further research, namely with larger double-blind randomized control trials from several geographic areas, will be needed to determine if these results are directly because of the procedure or secondary placebo effects. Given the results shown in these and other cases, we believe the prior to be the more likely scenario.

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