Pain Medicine Case Reports

ISSN 2768-5152
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Volume 7, Number 5, pp. 275-280

Successful Stellate Ganglion Block in Patients with Treatment Resistant Post-Traumatic Stress Disorder: A Case Series and Recent Literature Review

Miles R. Sanderson, MD, Usman Latif, MD, Dawood Sayed, MD, and Christopher M. Lam, MD

Background: Post-traumatic stress disorder (PTSD) is an increasing health concern in both those with and without previous military experience. There is a growing body of evidence for the use of stellate ganglion block (SGB), a procedure performed to treat pain conditions and cardiac arrythmias, in the treatment of PTSD. There have been multiple clinical studies, randomized and nonrandomized, that have demonstrated positive results for the use of SGB.

Case Report: In this case series, we present 3 patients with military background and treatment resistant PTSD who underwent SGBs. All 3 patients experienced a decrease in their clinical symptoms and improved quality of life.

Conclusion: Patients with refractory PTSD may benefit from SGB for treatment of their symptoms. PTSD symptoms may be sympathetically mediated, lending to the effect of SGB for symptom management. Data from recent clinical trials demonstrate a statistically significant reduction in PTSD symptoms when compared to sham procedures.

Key words: Case series, literature review, local anesthetic, Post-traumatic stress disorder, randomized control trial, stellate ganglion block, superficial cervical ganglion block, trauma

BACKGROUND

Post-traumatic stress disorder (PTSD) has become an increasing health concern in those with previous military experience and the public. The Diagnostic and Statistical Manual of Mental Disorders 5th edition (DSM-5) defines PTSD by 4 clusters of symptoms: persistent physiological arousal and reactivity, negative changes in mood and cognition, avoidance of trauma related stimuli, and intrusive reexperiencing of a traumatic event (1). Treatment for patients diagnosed with PTSD remains challenging due to active patient involvement and inclusion of multi-disciplinary teams. Despite advances in treatment of this pathological disorder, patients with severe refractory symptoms are often difficult to manage despite combinations of pharmacotherapy and psychotherapy.

The prevalence of PTSD ranges from 6.1 to 9.2% in the general adult population of the United States and Canada (2). Outside of military combat, multiple types of traumas have been linked to PTSD including sexual relationship violence, unexpected death of loved ones, childhood physical abuse, etc. (3). For those involved in military combat, studies have shown a link between extent of combat injury and development of PTSD symptoms (4).

From: Department of Anesthesiology and Pain Medicine, University of Kansas Medical Center, Kansas City, KS

Corresponding Author: Miles Sanderson, MD, E-mail: msanderson2@kumc.edu
Disclaimer: There was no external funding in the preparation of this manuscript.
Conflict of interest: Each author certifies that he or she, or a member of his or her immediate family, has no commercial association (i.e., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted manuscript.
Patient consent for publication: Consent obtained directly from patient(s).
Authors adhere to the CARE Guidelines for writing case reports and have provided the CARE Checklist to the journal editor.
Accepted: 2023-05-18, Published: 2023-09-30

In patients with newly diagnosed PTSD, trauma focused psychotherapy and pharmacotherapy (selective serotonin reuptake inhibitors) are recommended as first line treatments (5). Patient responsiveness to pharmacological treatment versus psychotherapy varies greatly and there are few individual predictors to whether a patient will experience a robust response to either therapy (6).

There is a growing body of evidence for the use of stellate ganglion block (SGB) in the treatment of PTSD. This procedure has been used to treat pain conditions since the 1940s. The first randomized, control trial (RCT) from Hanling et al 2016 suggested there to be no conclusive evidence between SGB and sham procedure in the treatment of PTSD (7). However, recent studies suggest that SGB may be effective in treating PTSD. Olmsted et al (8) in 2020 demonstrated a significant reduction over sham procedure in PTSD symptom severity over an 8-week timeframe. This and other trials suggest SGB may have a role in PTSD management (9-11). The purpose of our case series is to contribute to the current evidence and support the use of SGB in the treatment of PTSD.

Written informed consent from each patient was obtained for the following case series and accompanying figures.

CASE PRESENTATION

The first 2 patients were men. The first was 58-years-old and the second was 41-years-old. Each presented for evaluation and management of PTSD. Both patients have previous military experience. Initially they were managed with pharmacotherapy and prolonged exposure therapy. Despite escalating measures, they continued to have difficulty managing their symptoms of PTSD including nightmares/reliving trauma, irritability, and social avoidance. The 58-year-old man also experienced daily posterior headaches, consistent with occipital neuralgia, and persistent left arm pain. The 41-year-old man also experienced symptoms of intermittent rage, bad dreams, and neck pain.

The third patient is a 35-year-old woman, who presented for evaluation and management of her PTSD and fibromyalgia. Like the previous 2 patients, she served in the military, and failed conventional outpatient PTSD therapy. Her symptoms began shortly after her time in the military and worsened postpartum. She experienced wide-spread pain mostly focused on the right arm, right trapezius, and low back.

The first 2 patients underwent fluoroscopic guided SGB. An ipsilateral fluoroscopic view was obtained of the C6 vertebral body. The end plates were squared off and the transverse process, as well as neuroforamen, were identified in supine position with the patient facing the contralateral direction. The patient was prepped and draped in the usual fashion prior to identifying the proposed needle tract for safe access. Local anesthetic was injected along the planned needle tract. A 25-gauge spinal needle was advanced toward the medial aspect of the C6 transverse process unit and bone was contacted. Following negative aspiration, contrast was then injected to confirm the outline of the sympathetic chain without any signs of vascular uptake. Six mL of 0.25% bupivacaine with 10 mg dexamethasone and contrast was injected under live fluoroscopy (Fig. 1). The 41-year-old patient underwent a right SGB, and the 58-year-old underwent a left SGB due to previous symptom improvement following left SGB.

The third patient underwent an ultrasound (US)-guided right SGB. In supine positioning facing the contralateral direction, the patient was prepped and draped in the usual fashion. Under US visualization, the supraclavicular plexus was identified and traced up the neck until the C7 and C6 fibers were seen. The US continued to follow the C6 fibers until the C6 anterior and posterior tubercle were seen along with the transverse process. Local anesthetic was placed along the proposed tract and a spinal needle was advanced with US guidance with care avoiding the carotid artery until the stellate ganglion was reached before 4 mL of 0.25% bupivacaine and 10 mg dexamethasone was injected (Fig. 2). Provider preference accounts for: the difference in imaging modalities, use of dexamethasone, and volumes of local anesthetic used for this procedure.

All 3 patients developed Horner's syndrome within 10 minutes of the first injection, which is the classic sign associated with successful SGB as ganglia blockade would result in an ipsilateral sympathectomy (12). Our patients were monitored post procedurally for 30 minutes. No cardiorespiratory events or neurologic events were noted. Thus, the patients were stable and deemed safe for discharge.

All 3 patients endorsed reduction in their PTSD symptoms, along with reduction in their existing comorbidities (headaches, fibromyalgia, and intermittent rage) at their subsequent follow-up appointments. The first and second patient mentioned above returned at 3 months for a repeat SGB. Despite being performed on different sides, both patients experienced subjective improvement.

The 35-year-old woman at one-month follow-up reported significant improvement, however, was reexperiencing symptoms of PTSD and fibromyalgia. A repeat SGB was performed with 4 mL of 0.25% bupivacaine and dexamethasone with subjective improvement of her symptoms. At 3-month follow-up she continued to endorse improvement in her fibromyalgia symptoms and decreased PTSD symptoms. All her blocks were performed on the right side.

None of the patients noted any complications during the immediate follow-up period or at the time of reevaluation aside from Horner's Syndrome which self-resolved within 24 hours. All 3 patients reported subjective improvement in their PTSD symptoms as well as improvement in other co-morbid conditions at each subsequent follow-up.

Fig. 1. (Left) Spinal needle at the medial aspect of the C6 transverse process. (Right) Visualization of appropriate superior and inferior spread of contrast along the sympathetic chain.

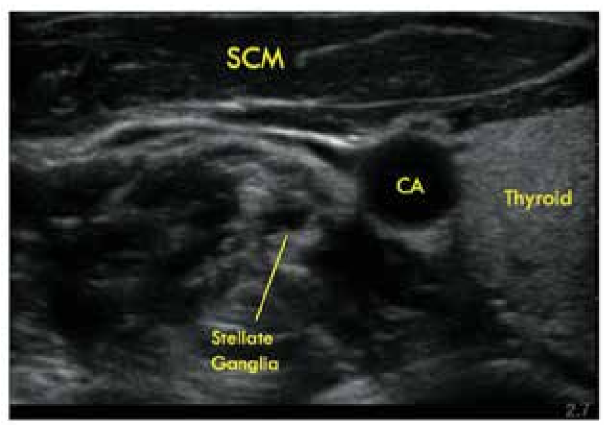

Fig. 2. Ultrasound image of stellate ganglia and other relevant anatomy: sternocleidomastoid muscle (SCM), carotid artery (CA) and thyroid tissue.

Recent Literature Review

The first psychiatric effects of SGB were reported in 1947 (13). Following this, several reports and trials have been conducted evaluating the effectiveness of SGB on PTSD. Since the last literature review in 2016 by Summers et al (14), multiple publications have emerged supporting the use of SGB in the treatment of PTSD (Table 1).

A RCT from Hanling et al (7), randomized 42 patients to receive either SGB or a sham procedure. This trial failed to show any statistically significant difference in clinical outcomes between the 2 groups. However, the methodology of this study was called into question. In the study, an active placebo was not utilized. This made blinding questionable as patients who did not develop Horner's syndrome would be able to tell they received placebo. The sample size of 42 patient is thought to be too small for a Phase 2 trial as most of these studies include 100-300 patients. Finally, the population selected may have a financial incentive to under-report treatment effectiveness as many were involved in medical board that determines disability (15).

The second RCTto evaluate the effect of SGB on PTSD on active-military personnel was conducted by Olmsted et al (8). This study used a 2:1 SGB to sham procedure ratio and randomized 113 patients (74 to SGB and 39 to sham procedure). The treatment arm then received right sided SGB at weeks zero and 2, while the control group received sham procedure at the same timepoints. A baseline assessment of clinical symptoms was obtained prior to initial intervention at week zero, followed by reassessment 8 weeks post-intervention. This study found that patients who underwent SGB had a larger reduction in symptoms than those who underwent sham procedure. This study differed from the previous RCT in that 2 SGBs were performed vs 1, larger sample sizing, increased statistical power and increase volume of ropivacaine (8). This was the first RCT to demonstrate a reduction in PTSD symptoms following SGB.

Recently, Mulvaney et al (16) performed a retrospec-

Table 1. Summary of relevant publications to SGB and PTSD

Authors	Study	Participants	Intervention	Outcome
Hanling et al.	RCT	42 patients Randomized 2:1 SGB to sham procedure.	Single SGB or sham performed at week 0.	No statistical difference between treatment and placebo
Olmsted et al.	RCT	113 patients Randomized 2:1 SGB to sham procedure	Paired right-sided SGB or sham procedure at weeks 0 and 2.	Statistically significant reduction in PTSD symptoms for those who underwent SGB vs sham
Mulvaney et al.	Retrospective analysis	10 patients unresponsive to right SGB	Left-sided SGB	90% response rate to left SGB and mean PCL-5 reduction was 28.3.
Hughey et al.	Cadaveric study	20 soft cured cadavers	Ultrasound vs fluoroscopy for SGB	Ultrasound injection resulted in accuracy of 90% while fluoroscopy 60%. Statistical significance not achieved.
Lipov et al.	Review Article	-	-	Local anesthetic can reduce perivascular catecholamines and ultimately PTSD symptoms.
Lipov et al.	Retrospective Cohort Study	327 patient records, 182 men and 145 women. Both military and non-military.	Cervical sympathetic blockade with either SGB or SGB followed by SCGB.	81% of patients experienced statistically significant reduction in PTSD symptoms. Both men and women had similar levels of symptom reduction post-intervention.
Peterson et al.	Non-randomized control trial	11 active-duty military personnel	SGB in combination with massed prolong exposure therapy for 2 weeks.	80% of patients had a reduction in symptoms and 50% no longer met diagnostic criteria for PTSD 1-month post intervention.

tive analysis on 205 patients and the utilization of left sided SGB on those who previously failed to respond to right sided SGB for reduction in PTSD symptoms. Out of the 205 patients that received right sided SGB, 20 patients did not respond to therapy. Ten of these patients went on to receive left-sided SGB, and of those patients 90% had clinical response to left-sided SGB. This study was limited in terms of length of follow-up as patients were reevaluated only one week after intervention. From this data it is difficult to assess whether this procedure would lead to long-term reduction in PTSD symptoms. However, it may offer further insight into management of patients who initially fail treatment with right sided SGB.

The exact mechanism to the effect of SGB on PTSD remains unknown. Lipov et al (17) previously proposed the effect of local anesthetic on nerve growth factor (NGF) leading to decreasing perivascular norepinephrine. Lipov et al (18) have since postulated that trauma may lead to increased deoxyribonucleic acid (DNA) methylation and increased levels of brain-derived neurotrophic factor (BDNF). This catalyzes sympathetic nerve sprouting and ultimately increased brain norepinephrine. Demethylation of DNA and reduction of NGF is accomplished through the application of local anesthetic leading to decreased sprouting, perivascular catecholamines, and ultimately reduction in PTSD symptoms (18).

Further retrospective analysis attempted to analyze the efficacy of cervical sympathetic blockade (CSB), and the effects on PTSD symptoms. In one retrospective analysis, CSB was defined as either SGB alone or subsequently followed by a superior cervical ganglion block (SCGB) after a 20-minute observational period with no improvement in symptoms. SCGB was performed similarly to SGB however targeting the ventrolateral aspect of the C3 vertebral body. This retrospective cohort analysis was carried out by Lipov et al (19) and reviewed 327 patient records assessing clinical severity at baseline and at a single timepoint between 7- and 30-days post-intervention. Of the 327 patient charts reviewed, 244 received both SGB and SCGB. This study demonstrated a significant clinical improvement in 81% of patients. There was no difference in outcomes between men and women who underwent CSB. Anatomically, the stellate ganglion sympathetic fibers follow the vertebral artery to the brain, while the superior cervical ganglion follows the internal carotid artery. The hypothesis suggests that by simultaneously targeting and blocking the specific areas of the brain where these fibers synapse, a more profound "rebooting" of the brain can be achieved, leading to a more significant reduction in symptoms associated with PTSD (19).

Among recent clinical trials, one conducted by Peterson et al (20) assessed the potential additive benefits of SGB with massed prolonged exposure therapy. In this nonrandomized clinical trial, 11 patients with military background underwent a single, right-sided SGB in combination with massed prolonged exposure therapy. Massed prolonged exposure therapy included 10 daily sessions of 90-minute therapy completed over a 2-week period. SGB was performed between sessions 1 and 2. Their results demonstrated a reduction in patient symptoms 1-month in for 80% of patients, while 50% of patients no longer met diagnostic criteria for PTSD. The synergistic effects observed are thought to be due to block timing and methodology of massed prolonged exposure therapy, and that these strong of results would not be observed by simply offering SGB in combination with trauma-focused behavioral therapy. Limitations of this study mainly lie in the small sample size tested and nonrandomization, which restricts the ability to allow for generalization of results to larger populations (20).

Our patients in this study experienced a significant reduction in PTSD symptoms following SGB. No patients experienced adverse events from the procedure. Despite this, care needs to be expressed when deciding whether to utilize SGB for the treatment of PTSD versus noninterventional methods.

CONCLUSION

We hope this case series and literature review contributes to evidence favoring the use of SGB for PTSD therapy. Continued research into the exact mechanism of action of SGB on PTSD would prove beneficial as to define the underlying pathophysiology of PTSD. The available literature points to a sympathetically mediated pathophysiology explaining why a sympathectomy would treat the symptoms. A better understanding may open the door for better pharmacologic therapies and other less invasive interventions to safely treat this condition, including deep transcranial magnetic stimulation (21). Further, most studies to date involve military personnel, and clinical trials involving those outside the military community may prove beneficial as to the application of SGB to the general population with PTSD. Further studies are needed to fully evaluate this condition and its treatment allowing for earlier implementation of SGB for PTSD therapy.

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