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The Effectiveness and Safety of Stellate Ganglion Block in the Treatment of Symptoms from Long COVID-19: A Pilot Study

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ABSTRACT *~* ***Purpose:*** *Pilot study to evaluate the safety and effectiveness of stellate ganglion blocks in the treatment of symptoms related to long COVID infection.* ***Materials and Methods:*** *A total of 17 patients who underwent stellate ganglion block for the treatment of their long COVID symptoms were included. COMPASS-31, GAD-7, PCL-5, and Fatigue Severity Score (FSS) pre and post intervention surveys and data on baseline heartrate and post- block heart rate recorded in the EMR.* ***Results:*** *A total of 94% of patients reported moderate-to-severe autonomic dysfunction pre-procedure as measured by COMPASS-31. All patients reported some degree of symptomatic improvement from the block. Specifically, patients had significantly lower FSS scores (P = 0.002) and heart rate post-procedure (P = 0.008). Although the decrease in PCL-5 scores after the procedure was clinically meaningful, this change was not statistically significant (P = 0.159). No significant difference was found in pre and post procedure GAD-7 scores (P = 0.101).* ***Conclusions:*** *Stellate ganglion block is a safe, low-risk, minimally invasive, and effective procedure in the treatment of symptoms for long COVID. It should be evaluated as an adjunctive treatment of select patients in this population.* Psychopharmacology Bulletin. *2024;54(4):8–17.*

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Introduction

The COVID-19 pandemic has left over 1,000,000 dead and up to 30% of those infected with long term effects of the disease in the United States, known as long COVID.[1] Long COVID often manifests as neuropsychiatric sequelae including post-traumatic stress disorder, depression, anxiety, and cognitive symptoms.[2] Autonomic dysfunction is also prevalent in long COVID, with many patients meeting criteria for postural orthostatic tachycardia syndrome (POTS) and inappropriate sinus tachycardia.[3] These resulting conditions are difficult to treat and can leave people unable to work, drive, or participate actively in society. While it is unclear exactly how many patients have debilitating long COVID, when combining Household Pulse Survey (HPS) from the Federal Census Bureau with data from the CDC, annual cost of those lost wages alone is around $170 billion a year and potentially as high as $230 billion.[4]

Current conservative treatments aimed at the treatment of symptoms of long COVID include, but are not limited to: pulmonary therapy, physical therapy, pharmacology to manage sympathetically mediated tachycardia and postural orthostatic hypotension (POTS syndrome), low dose naltrexone for brain fog, anxiolytics and stimulants for management of worsening anxiety/PTSD and fatigue, and many more. No one treatment has been validated and there is currently no standard protocol for the treatment of the debilitating symptoms associated with this disease.[5,6]

A stellate ganglion block is a minimally invasive adjunctive procedure that has been utilized as an adjunct treatment for patients with complex regional pain syndrome (CRPS), refractory ventricular tachycardia as well as for post-traumatic stress disorder (PTSD).[7–11] Since we see the effects of sympathetic overactivation and PTSD in patients with long COVID, it is important to understand the role stellate ganglion blockade in patient treatment and symptomatic control related to these pathologies.[12,13]

Ventricular tachycardia and electric storm are difficult conditions to treat. Recurrent ventricular arrhythmias (VA) and electric storm are associated with increased sympathetic tone, and patient morbidity.[14,15] There have been studies in the literature supporting the efficacy of unilateral versus bilateral stellate ganglion block in reducing the need for external or internal defibrillation in this patient group.[8] This procedure, as an adjunct to medications and failed ablations, can even lead to resolution of VA, allowing patients to be discharged from the hospital.

PTSD can be a debilitating disorder that affects up to 20% of combat veterans and approximately 6% of the general population.[9,10] Stellate ganglion blocks have been performed as a successful adjunctive therapy for PTSD since the 1990s.[10,11] The proposed method of action is that

PTSD results in sympathetic hyperarousal and that blocking the stellate ganglion allows for a 'sympathetic reset', resulting in statistically significant decrease in PTSD symptoms-notably decreased irritability, improved concentration, and improved sleep.[9–11]

Given symptoms of sympathetic dysregulation implicated in long COVID, there have been a few small case series that tried a stellate ganglion block in patients with long COVID.[16–18] These patients had improvement in many of their symptoms, allowing them to return to society. In this study, we will evaluate the safety and effectiveness of stellate ganglion blocks on symptoms related to long COVID with a focus on the neuropsychiatric and autonomic sequalae of long COVID. We hypothesize that stellate ganglion blocks will improve patients' symptoms and have a positive impact on patient quality of life.

Materials and Methods

Methods of Selection

This was a single-institution retrospective observational study of patients who underwent a stellate ganglion block between October 2022–May 2023 as part of their care for long COVID symptoms. To be considered for a stellate ganglion block, patients had to be diagnosed with symptoms consistent with sequalae of long COVID by a board-certified Physical Medicine and Rehab (PM&R) physician. Patients were diagnosed with long COVID if they had new, recurring, or ongoing symptoms more than 4 weeks after an acute COVID-19 infection with documented positive polymerase chain reaction or antigen test around the time of acute infection.

Prior to the initiation of the study, Institutional Review Board (IRB) approval was obtained for a retrospective chart review. Inclusion criteria included patients over the age of 18 years diagnosed with long COVID who had incomplete symptomatic relief related to PTSD, anxiety, fatigue, and dysautonomia despite conservative management. Patients were excluded from the study if they had a prior stellate ganglion block without documentation of symptoms pre and post intervention. A total of 20 patients met inclusion criteria for the study. The STROBE checklist for cohort studies was used to ensure transparent reporting.

Pre and Post Intervention Symptom Evaluation

Data collected for the electronic medical record for evaluation included surveys completed by patients at the time of the initial clinic visit, approximately two to three weeks prior to their subsequent procedure, and at the one-week post-procedural clinic visit. Data was also collected

on a subset of patients whom had clinic visits at one, two and three-months post-procedure. The surveys included were COMPASS-31,[19,20] PCL-5,[21] GAD-7,[21] and the Fatigue Severity Scale (FSS).[22] Data was also collected regarding patient demographics, patient heart rate at pre and post procedure clinic visits, operative notes detailing the block cocktail and side block was performed, and any documentation of procedural or post-procedure complications.

Procedure: Stellate Ganglion Block

Stellate ganglion blocks were performed by either a board-certified Interventional Radiologist or Pain Management physician. Image guidance with any combination of ultrasound/CT and sedation was utilized for the procedure based on operator preference.

Patients were brought to the procedure room and placed supine on the table. Each patient was prepped and draped in usual sterile fashion. Ultrasound was used to identify the location of the jugular vein, carotid artery, vertebral artery, esophagus, and lung relative to the stellate ganglion, so a safe trajectory path could be planned. Local anesthetic was administered and moderate sedation was utilized per patient preference.

Based on operator preference, under continuous US guidance, a 22 or 25-gauge Chiba need was advance to the region of the stellate ganglion along the transverse process of C6 or the origin of the T1 Rib, with or without the adjunctive use of CT to confirm needle placement. Once needle placement was confirmed, 4–10 cc of 0.25% bupivacaine with or without a steroid was injected into the region of the stellate ganglion. The needle was removed from the patient and a sterile dressing was placed upon visually confirming no bleeding or hematoma formation was occurring at needle insertion site. Patients were monitored for one-hour post-procedure to recover from sedation and for potential complications that can occur in the immediate perioperative period such as hoarseness, dysphagia, and Horner's syndrome. Patients were subsequently discharged home and followed up in clinic one to three weeks later to assess for symptomatic improvement.

Statistical Methods

Descriptive analysis was performed and results were reported as mean and standard deviation (SD) or median and interquartile range (IQR) for continuous variables, and frequency and percentages for categorical variables. Paired sample *t*-test or the Wilcoxon signed-rank test as its non-parametric equivalent was used for the comparison of patient's pre- and post-intervention heart rate and scores on the COMPASS 31,

PCL-5, GAD-7, and FSS surveys. All statistical tests were performed at 0.05 level of significance and conducted using SAS statistical software (version 9.4, the SAS Institute, Cary, NC).

Results

Of the 20 patients that met inclusion criteria for the study, three patients were lost to follow-up, leaving 17 patients to be included in the statistical analysis. Patient demographics detailed in Table 1. All 17 patients completed pre-procedure COMPASS 31, GAD-7, and FSS surveys. Sixteen patients completed post-procedure COMPASS 31, GAD-7, and FSS surveys and 1 patient completed only the COMPASS 31 post-procedure. Of these 17 patients, 14 patients had documented heart rates pre and post intervention in the EMR and a subset of 10 patients also completed pre and post PCL-5 surveys. Of these 17 patients, 3 patients had the addition of a steroid to their block, while 14 patients had a local anesthetic injected only. A total of 8 patients, two of which had steroids added to their blocks, had clinic follow-up at 1, 2, and 3 months with documentation on maintenance of symptomatic relief.

TABLE 1

Patients' Demographic, Pre-Procedure Clinical and Block Characteristics (N = 17)

Sex, n(%)	
Male	6 (35.3)
Female	11 (64.7)
Pre-procedure compass 31 score[a], mean ± SD	57.2 ± 23.9
orthostatic intolerance	22.7 ± 13.6
Vasomotor	1.5 ± 1.7
secretomotor	12.0 ± 6.8
gastrointestinal	14.4 ± 6.1
bladder	2.3 ± 1.6
pupillomotor	2.8 ± 1.6
Pre-procedure compass 31 score > 20[a] (i.e., moderate to severe autonomic dysfunction), n(%)	15 (93.7)
Pre-procedure compass 31 score > 40[a] (i.e., severe autonomic dysfunction), n(%)	13 (81.2)
Blocked side, n(%)	
Right	10 (58.8)
Left	6 (32.3)
L/R	1 (5.9)
Block Cocktail, n(%)	
Bupivicaine Only	14 (82.4)
Bupivicaine + Steroids	3 (17.6)

[a]Data is missing for 1 patient.

Technical success- as defined by safe completion of the procedure without need for immediate further intervention- was achieved in all 17 patients. An approximately equal number of patient blocks were performed with ultrasound guidance only (n = 9) versus CT and ultrasound guidance (n = 8), as well as a right (n = 10) versus a left (n = 7) stellate ganglion block. Using the Society of Interventional Radiology (SIR) adverse event (AE) classification system, there were no major or minor complications. Two patients experienced unilateral Horner's syndrome, which can be expected post stellate ganglion block, with resolution of symptoms within 1 week after intervention.

Pre-procedure COMPASS-31 scores showed 94% of patients reported moderate autonomic dysfunction and 81% reported severe autonomic dysfunction (Table 1). All patients reported some degree of symptomatic improvement from the block. Specifically, patients had significantly lower FSS scores ($P = 0.002$) and heart rate post-procedure ($P = 0.008$) (Table 2, Figure 1). There was no statistically significant difference in PCL-5 scores pre and post procedure ($P = 0.159$) but there was a clinically significant difference with a drop in overall scores an average of 5 points, dropping scores below the clinical threshold for PTSD diagnosis (Table 2, Figure 1). No significant difference was found in pre and post procedure GAD-7 scores ($P = 0.101$) (Table 2, Figure 1).

In the subgroup (n = 8) of patients followed at 1, 2, and 3 months post-procedure, one patient reported no symptomatic improvement post-block. Out of the 7 patients who had symptomatic improvement post-block, maintenance of initial documented symptomatic relief from surveys was maintained for 6–11 weeks post-procedure. Two patients in this subgroup received steroids as a part of their block and reported maintenance symptomatic relief for 9 and 11 weeks, while the remaining patients (n = 5) reported maintenance of symptomatic relief for 6–8weeks (n = 5).

TABLE 2

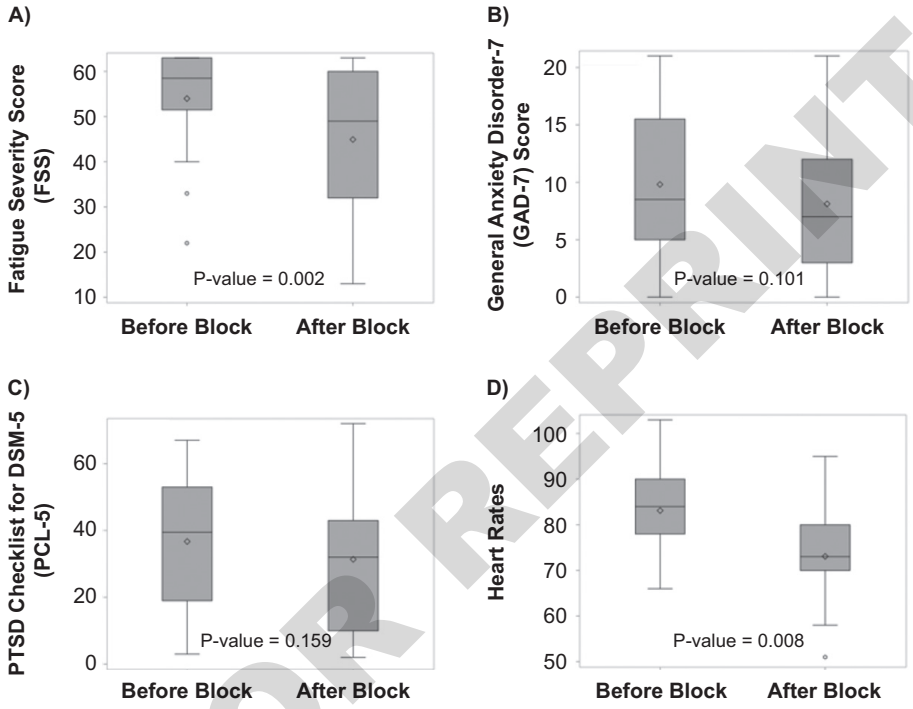
Comparison of the Severity of Patients' Symptoms and Heart Rate Pre- and Post-Stellate Ganglion Block procedure

	PRE-PROCEDURE	POST-PROCEDURE	*P*-VALUE
FSS[a], median (IQR)	58.0 (51.5, 63.0)	49.0 (32.0, 60.0)	0.002
GAD-7[a]	9.8 ± 6.2	8.1 ± 6.1	0.101
PCL-5[b]	36.7 ± 20.8	31.4 ± 23.4	0.159
Heart Rate[c]	83.1 ± 10.1	73.1 ± 11.7	0.008

Data presented as mean ± SD, otherwise as indicated. [a]Missing pre-procedure data for 1 patient. [b]Missing pre-procedure data for 3 patients and post-procedure data for 6 patients. [c]Missing post-procedure data for 3 patients.

FIGURE 1

Comparison of Patients' Fatigue Severity (FSS), General Anxiety Disorder-7 (GAD-7), Post-Traumatic Stress Disorder (PTSD) Checklist for DSM-5 (PCL-5) Scores, and Heart Rates Pre- and Post-Stellate Ganglion Block procedure



Discussion

In this small retrospective study, all patients reported subjective symptomatic relief of all their long COVID symptoms with a stellate ganglion block and a clinically significant number of patients had measurable objective improvement in their fatigue symptoms and elevated heart rate related to long COVID. Additionally, a subset of patient who were followed up to three months procedure reported maintenance of their symptomatic relief for 6–11 weeks. Results on longevity of block should be interpreted with prudence however, as only 47% of patients were followed up for three months and of those patients, two received blocks with the addition of a steroid.

There were no complications or untoward effects from the procedure in any patient. While there was not statistically significant improvement in symptoms related to PTSD, this study had a 5-point decrease in PCL-5 score post intervention. The DSM-IV suggests that any change in assessment between 5–10 points suggests a reliable change in

symptom severity and furthermore, any change greater than five points should be viewed as a meaningful response to treatment. The change of only 5 points seen in this study may be reflective of a small sample size related to inadequate data collection (n = 10 vs n = 17 for other surveys) and may have been more significant with more data.

We acknowledge the limitations of this study including the retrospective nature of the study, small sample size, lack of a control group, and incomplete survey data on several patients. Practitioners used two different imaging techniques to perform the block, either ultrasound only or CT in combination with ultrasound. Since there was an approximately equal number of patients in each group, the technique employed to perform the block likely does not affect the effectiveness, however, this could not be looked at in detail due to the small sample size of the study. While we investigated the descriptive statistics on whether patient results could have been affected by factors to include the addition of steroid to the block, technique used to perform the block, and on which side the block was performed, our relatively sample size limited our ability to account for possible variations in our findings by these factors. As there have been studies on patients with PTSD showing differences in response to stellate ganglion block based on side, further larger scale studies need to be performed to see if side blocked in patients with long COVID affects effectiveness of the procedure with respect to not only PTSD symptoms but also dysautonomia symptoms (11). Furthermore, since steroids were used in only three patients from the study and have short- and long-term effects on physiology, it is important to determine whether or not steroids are truly necessary for longevity of symptomatic relief in this patient population who may need repeat blocks/interventions.

This study shows that a stellate ganglion block is a safe, effective procedure that can be used as an adjunctive treatment in patients with long COVID. Many of the symptoms that occur in this patient population align with symptoms of other disease/medical states that have been successfully treated with stellate ganglion blocks. With improvement in long COVID symptoms related autonomic dysfunction–measured by improvement in patient heart rate post block- our study suggests that a stellate block might be a useful adjunctive treatment for long COVID patients with dysautonomia. The small study size precluded further subgroup analysis of this population and this observation should be noted just as such.

Conclusion

Stellate ganglion blocks are a safe and may be an effective procedure in the treatment of symptoms related to long COVID infection. ✤

Conflict of Interest (for all authors)

Grant H. Chen—Consultant for SPR Therapeutics.
Jamal Hasoon—Consultant for SPR Therapeutics.
Alexa Levey—Consultant for Focused Cryo Inc.

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