

## Research Article

# Comparison C6 Stellate Ganglion versus C6 and C4 Cervical Sympathetic Chain Blocks for Treatment of Posttraumatic Stress Disorder (PTSD): Analysis of 147 Patients

Sean W. Mulvaney<sup>1,2\*</sup>, Kamisha E. Curtis<sup>2</sup>, Tamara S. Ibrahim<sup>2</sup>

<sup>1</sup>Department of Military and Emergency Medicine, Uniformed Service University, USA

<sup>2</sup>Regenerative Orthopedic and Sports Medicine, Maryland, USA

**\*Corresponding author**

Sean Mulvaney, Regenerative Orthopedic and Sports Medicine, 116 Defense Hwy, suite 203, Annapolis, MD 21401, USA, Tel: 410-505-0530; Email: drsean@rosm.org

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• Stellate ganglion block; Post-traumatic stress disorder; PTSD; PTSI; Cervical sympathetic chain block; Two-level block; Two level sympathetic block; 2LSB; Sympathetic chain block; Ultrasound guided

**Abstract**

**Objective:** Determine whether a two-level cervical sympathetic chain block may be more effective than a standard C6 level stellate ganglion block (SGB) for the treatment of posttraumatic stress disorder (PTSD).

**Background:** A right-sided SGB has many medical publications supporting its safety and efficacy for the treatment of PTSD. However, in clinical practice, some patients do not respond to a C6 level SGB as anticipated. Currently, there are no published reports describing a two-level sympathetic block (2LSB) as a treatment modality. Thus, the purpose of this investigation is to initially assess safety and efficacy of this novel procedure as compared to the standard procedure.

**Methods:** The PTSD Checklist (PCL-5) is routinely collected for patients prior to SGB or 2LSB for PTSD. We retrospectively evaluated baseline (T0) and 4 weeks (T1) PCL-5 scores in post-SGB/2LSB in our center.

**Results:** One-hundred and forty-seven of 328 consecutive subjects underwent SGB (group 1) or 2LSB (group 2), in 51 females 96 males, (17 to 75 years). The mean improvement in PCL-5 scores at T1 for the SGB was 25.2 (20.40246-29.84997 CI 95%) ( $p < 0.001$ ) (N = 103) and 2LSB was 31.78 (26.05481-37.49065 CI 95%) ( $p < 0.001$ ) (N = 44). Although the improvement was greater in group 2, there was no significant difference between group 1 and 2 at T1. There were no adverse events or complications reported in either group.

**Conclusions:** Single SGB and 2LSB were both effective in treating PTSD. A 2LSB is safe and may be more effective than a standard SGB in the treatment of PTSD. Further research on this treatment modality is required before conclusions on the effectiveness of a 2LSB for the treatment of PTSD symptoms can be made.

**INTRODUCTION**

Post-traumatic stress disorder (PTSD) is defined by the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) as a pathologic trauma and stressor disorder that occurs in some individuals following exposure to severe trauma. Right-sided SGB has been described in 13 peer-review medical publications [1-12] including a level 1 RCT [13], with consistent safety and efficacy in the successful treatment of PTSD. All publications have been using a standard right-sided C6 level SGB. In clinical practice, some patients did not improve with an SGB as anticipated. Currently no PubMed indexes report on the use of higher-level cervical blocks for the treatment of PTSD. Additionally, there are no descriptions in the medical literature describing a two-level block sympathetic chain block as a treatment modality for any condition.

There is considerable anatomic variation in the both the course of the cervical sympathetic chain as well as the location and anatomic plane of the middle cervical ganglion. Furthermore,

there is also considerable anatomic variation in the sympathetic chain components merging with peripheral nervous system, in this case the superficial and deep cervical plexus as well as with the brachial plexus [14-16]. In our clinical practice, some patients failed to respond to an SGB although they appeared to have a similar clinical presentation as other candidates that responded well. To clinically account for this normal anatomic variation, it seemed plausible that treating two levels of the sympathetic chain (2LSB) would be better than using a single SGB and could possibly account for the difference in clinical observations.

**MATERIAL AND METHODS****Patients**

The population screened for treatment in this private practice clinic was diverse in age and sex as well type of trauma. The age range of our treatment population was 17 to 75 years old. Females made up 23% (10 of 44) of the 2LSB group and 40% (41 of 103) of the SGB group. Our patients reported multiple sources

of trauma which included: military/combat-related (58 of 144), first responder related trauma, (EMS, police and firefighters) (9 of 144), childhood trauma (10 of 144), sexual assault (1 of 144) and trauma not specified (69 of 144). Duration of symptoms ranged from 1 year to 53 years (Vietnam veteran, Tet offensive, 1968). All individuals had a minimum PCL-5 baseline score of 40. In the normal course of clinical practice and follow-up the following data was routinely collected to facilitate patient care on patients seeking care for PTSD: baseline PCL-5 scores (T0), and 4 weeks (T1) post-SGB PCL-5 score. Prior to review, institutional review board approval was obtained (#IRCM-2020-250) to de-identify data and compare the PCL-5 scores at T0 and T1 for the two groups: groups 1(SGB) and 2 (2LSB). The primary end point was the comparison of the mean improvement in PCL-5 scores from baseline to one month between the groups. All procedures were performed at an established musculoskeletal practice performed by the same anesthesia/pain fellowship-trained physician who has performed over 1400 ultrasound-guided SGBs.

## Treatment

Detailed informed consent was obtained prior to all procedures for either an SGB or 2LSB. The unседated, awake patient was placed in the supine position with the head rotated slightly to the left with monitoring per clinic protocol. The skin over the anterior and right-side neck was widely cleaned with chlorhexidine-isopropyl alcohol preparation and 2 grams of sterile ultrasound gel was applied. The right-side anterior neck was scanned using a broadband linear transducer (8-13 MHz, GE Logic e, Wauwatosa, WI, USA) from the level of the 7<sup>th</sup> to the 4<sup>th</sup> cervical vertebrae in transverse view. The C-6 level was confirmed by palpation of the cricoid membrane as well as comparing the appearance of the C-4, C-5, C-6, and C-7 anterior tubercles. A distinct advantage of using ultrasound-guidance is the ability to use power Doppler, which was used to identify vasculature in the planned needle track, and specifically the track of the vertebral artery or any aberrant vessels. The skin at injection site on the lateral neck was anesthetized with 1 ml of 1% lidocaine (Hikma Pharmaceuticals, London, UK) buffered with 8.4% sodium bicarbonate (Hospira, Inc, Lake Forest, IL, USA). Utilizing an in-plane approach, under real-time ultrasound guidance either a 22-gauge 2.75-inch needle or a 25-gauge 2-inch needle was placed just dorsal to the ventral fascia of the longus colli, medial to the longus capitus and approximated to the cervical sympathetic chain. After attempted aspiration, while monitoring the patient, 0.5 ml of 0.5% ropivacaine (Hospira, Inc, Lake Forest, IL, USA) was injected, and after observing the patient for 30 seconds, a second 0.5 ml aliquot was injected. The patient was monitored for an additional 30 seconds. After the patient verbally confirmed an absence of any concerning symptoms, an additional 7-8 ml of 0.5% ropivacaine was slowly injected over 1 minute for a total injection volume of 8-9 ml for a single-level block, (7 ml at the C6 level for a 2LSB). When a 2LSB was performed, the 4<sup>th</sup> cervical vertebrae level was performed in the same fashion with 3-4 ml of the same long acting local anesthetic. The needle was withdrawn, the ultrasound gel was wiped off with gauze and an adhesive bandage was placed on the injection site(s). Specific precautions were given, including the presence of a temporary Horner's syndrome, the possibility of a temporary dysphonia, globus sensation or dysphagia. Both before and after the procedure, the patient was specifically counseled on potential for and signs of

life-threatening adverse effects, including worsening neck pain which may indicate hematoma formation, shortness of breath which could indicate pneumothorax or temporary blockade of the phrenic nerve, or seizure which would indicate inadvertent intravascular uptake of the local anesthetic. All procedures were well-tolerated. At five minutes post-procedure, the patient was asked to sit up on the side of the bed and the Horner's syndrome was independently quantitatively graded by two experienced graders using previously published scale [17]. All Horner's responses were graded a minimum 4 out of 6 possible points (a dense and obvious sympathetic blockade measuring objective findings of ptosis, miosis and scleral injection). The patient was then returned to the supine position and monitored for an additional 30 minutes and discharged.

## Primary outcome metric

The PTSD Checklist (PCL-5) is a 20-item self-report correspondent measure of the DSM-V criteria used to screen individuals for PTSD symptoms and monitor post-treatment symptom progression. The checklist possesses strong test-retest reliability, internal consistency, and diagnostic utility against clinician-administered PTSD scale for DSM-5 (CAPS-5) [18,19]. Respondents rate how much they were bothered by a given PTSD symptom in the past month using a five-point scale ranging from "Not at all" to "Extremely". Items are summed to provide a total severity score ranging from 0 indicating "no symptoms" to 80 indicating "severe symptoms". A score of 31-33 is accepted as a valid diagnostic cut-off score and is used as a provisional PTSD diagnosis for veteran and undergraduate populations [20,21]. Scores lower than 33 may indicate a patient's symptoms are sub threshold for PTSD [22]. The National Center for PTSD states a 5-point score decrease is the minimum threshold to determine an adequate response to treatment while at least a 10-point score improvement is considered clinically meaningful. While these reliable and clinically significant changes are based on evidence for the 17-item PCL for DSM-IV, it is expected that change scores for the PCL-5 will be in a similar range [23,24]. For this study, patients with PCL scores of 40 or greater were included in the data set. A patient was deemed responsive to the intervention with a total PCL-5 score decrease of 10 points from pre-procedure to follow up testing.

## Data analysis

Statistical analysis was performed co-author KC. An unpaired t-test was used to compare the baseline means for significance, which proved their difference is insignificant. A Welch's Two-Sample t-test was used to compare the mean score changes. The R (Vienna, Austria) statistical package R Studio (Boston, USA) was used for the computation of the means and confidence intervals.

## RESULTS

### Stellate Ganglion Block (SGB) (n=103)

A total of 103/205 (50%) patients submitted follow up data at one-month post-block. Of these 103 patients, 80.58% improved by over 10 points on the PCL-5, mean scores improved in group 1 by 25.2 points (t=10.5) (20.40246 to 29.84997 CI 95%) (p < 0.001) (Table 1). The mean baseline score for patients who received an SGB was 60.9 (11.4 sd) and the mean score at one month was 35.7. There was a 25.2-point score improvement with an SGB, a number well above the accepted clinically significant

**Table 1:** PCL-5 Scores at Baseline and One Month .

	Baseline	One Month	Δ PCL-5 Score at One Month
C6 (n=103 patients)	60.9	35.7	25.2
C4-C6 (n=44 patients)	58.5	26.72	31.78

\*The difference between the change in mean scores of an SGB and 2LSB is 6.58 at one month.

change [23,25] some of the non-responders opted to have a left-sided block C-6 block, (per published guidelines) [17] and experienced significant improvement.

#### Two-Level Sympathetic Block (2LSB) (n=44)

Of the 44 patients who received a 2LSB and provided one-month PCL-5 scores, 37 (85.71%) improved by over 10 points. The mean baseline score was 58.5 (10.6 sd) and the mean score of group 2 at one month was 26.72. The mean improvement in PCL-5 scores over one month was 31.78 ( $t=11.1$ ) (26.05481-37.49065 CI 95%) ( $p < 0.001$ ) (Table 1).

#### Differences in PCL-5 Scores at One Month

The mean baseline scores for each group were compared to one another and their difference was insignificant ( $t=1.23$ ) ( $p=0.22$ ) (-1.490190 to 6.296016 CI 95%). Both the SGB and the 2LSB experienced significant improvement in their symptoms. The (single-level) SGB group responded with a mean improvement in PCL-5 score of 25.2 points. While this exceeds the accepted clinically significant improvement, the 2LSB group responded with an even greater improvement of 31.78 points [23]. As verified by calculating the difference of each group's baseline and one-month scores, the 2LSB group experienced a 6.58 point greater improvement than the SGB group. This difference in mean change between the two groups was tested and found to be insignificant ( $t=1.95$ ) (-0.1287868 to 13.4218142 CI 95%) ( $p=0.054$ ).

#### Safety and tolerability

There were no significant adverse events in the 338 SGBs or 2LSBs performed (275 SGB, 63 2LSB) in this 7-month period. There were 3 cases of temporary headache lasting several hours. There was one self-limited migraine headache within the 24 hours after the SGB by a patient with a history of migraines. There were 2 cases of self-limited soreness at the injection site. Although not considered an adverse event in SGB, about 15% of patients had temporary hoarseness or globus sensation associated from anesthetic spread and inadvertent block of the recurrent laryngeal nerve. All mild adverse effects were resolved within 24 hours. Interestingly, 5 patients reported significant improvement or resolution of their tinnitus.

#### DISCUSSION

The purpose of this case series is to compare the effectiveness of blocking the sympathetic cervical chain at one-level versus two-levels. To assess this hypothesis, patient data was separated into two groups: SGB (group 1) and 2LSB (group 2). PCL-5 scores for patients in group 1 were collected over a time period of six months (August 2019 to February 2020) at baseline and one month. Similarly, data was collected from group 2 over a three-month time period (January 2020 to April 2020). Patients

were screened and only those with baseline scores  $\geq 40$  were included in the analysis. The baseline PCL-5 scores of patients who provided follow-up ranged from 40 to 80 points. The mean baseline score for each group differed by 2.4 points (C6: 60.9 and C4-C6: 58.5), the differences were not significant. Therefore, we cannot reject the notion that there is no difference in outcomes between the two groups. There are likely patient factors and/or other heterogeneity within the groups which must be further explored.

Lack of desired results is what prompted alternative approach to management of these patients. In the initial patients that failed to improve after SGB, a 2LSB was attempted. The initial attempts utilizing a 2LSB were successful in cases where an SGB failed. In clinical practice, we observed that patients significantly improved when a 2LSB was done, especially those with more severe symptoms. Our initial anecdotal feedback supported that a 2LSB may be a more potent technique for treating PTSD. Over the course of three months, we gradually adopted the 2LSB as the standard. The 4<sup>th</sup> cervical level is approximately at the angle of mandible and was chosen for the second, more cephalad location on the cervical sympathetic chain because it is a potentially safer cervical level with ultrasound guidance. This would theoretically make the 2LSB more straight-forward to safely reproduced by other physicians.

This study reinforces that cervical sympathetic blockade has a profound and immediate effect on posttraumatic symptoms and should be considered as a valuable adjunct in the treatment of all patients with PTSD. Both an SGB and a 2LSB were both safe and effective in the treatment of PTSD symptoms. We explored a novel variation of this proven technique. Based on our limited clinical observations, a right-sided two-level cervical sympathetic chain block (2LSB) administered at C6 and C4 levels appears to be safe and may be more effective than a standard SGB in the treatment of PTSD symptoms. This is the first clinical report of the use of a two-level cervical sympathetic chain block as a treatment modality and may have relevance for other conditions for which an SGB is indicated. There is a significant anatomic variation in the course of the cervical sympathetic chain as well as in the location of the middle cervical ganglion which provides a reasonable explanation for the observed benefits of a 2LSB.

#### Limitations

This is a retrospective case series and can only show a clinically observed relationship between improved patient performances with a 2LSB versus an SGB. The authors acknowledge the main limitations of this study were patients lost to follow-up as well as limited time of follow-up (1 month). Out of 338 consecutive one or two-level procedures performed between August 2019 and March 2020, 191 patients were lost to follow-up. There was a difference in the total volume of local anesthetic used between the two procedures, with the SGB using 8-9 milliliters and the 2LSB using 10-11 milliliters of 0.5% ropivacaine. It is possible this volume difference, though small, may account for some of the observed differences between the two groups.

There is considerable normal anatomic variation in the course of the cervical sympathetic chain, specifically, in both the anatomic plane it traverses and the location of the middle cervical

ganglion. Due to these common anatomical variations in the cervical sympathetic chain, we hypothesize that a 2LSB routinely achieves a more effective concentration of 0.5% ropivacaine at the relevant sympathetic neurons and fibers in the middle and / or superior cervical ganglion communicating with cortical regions that mediate PTSD symptoms.

## CONCLUSION

Single SGB and 2LSB were both effective in treating PTSD. A 2LSB is safe and may be more effective than a standard SGB in the treatment of PTSD. Further research on this treatment modality is required before conclusions on the effectiveness of a 2LSB for the treatment of PTSD symptoms can be made.

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## ETHICS APPROVAL

The IRB for this paper was the Institute for Regenerative and Cellular Medicine IRB in Santa Monica, CA, USA

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