

Efficacy of Stellate Ganglion Blockade for the Management of Type 1 Complex Regional Pain Syndrome

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Introduction: The purpose of this study was to examine the efficacy of stellate ganglion blockade (SGB) in patients with complex regional pain syndromes (CRPS I) of their hands.

Methods: After IRB approval and patient informed consent, 25 subjects, with a clinical diagnosis of CRPS I of one hand as defined by the International Association for the Study of Pain (IASP) criteria, had three SGB's performed at weekly intervals. Laser Doppler fluxmetric hand perfusion studies were performed on the normal and CRPS I hands pre- and post-SGB therapy. No patient was included in this study if they used tobacco products or any medication or substance that could affect sympathetic function. The appropriate parametric and nonparametric data analyses were performed and a p value <0.05 was used to reject the null hypothesis.

Results: Symptom onset of CRPS I until the initiation of SGB therapy ranged between 3 to 34 weeks. Following the SGB series, patient pain relief was as follows: group I, 10/25 (40%) had complete symptom relief; group II, 9/25 (36%) had partial relief and group III, 6/25 (24%) had no relief. The duration of symptoms until SGB therapy was: group I, 4.6 ± 1.8 weeks, group II, 11.9 ± 1.6 weeks and group III, 35.8 ± 27 weeks. Compared with the normal control hand, the skin perfusion in the CRPS I affected hand was greater in group I and decreased in groups II and III.

Discussion: The results of our study demonstrate that an inverse relationship exists between hand perfusion and the duration of symptoms of CRPS I. On the other hand, a positive correlation exists between SGB efficacy and how soon SGB therapy is initiated. A duration of symptoms greater than 16 weeks before the initial SGB and/or a decrease in skin perfusion of 22% between the normal and affected hands adversely affects the efficacy of SGB therapy.

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Reflex sympathetic dystrophy, now referred to as complex regional pain syndrome (CRPS) types I and II, can be difficult to treat. Dysfunction of the sympathetic nervous system is observed in patients affected with CRPS.^{1,2} Sympathetic nervous system dysfunction causes alterations in skin temperature in experimental models,³ which is believed to be attributed to changes in microcirculatory disturbances as a result of extensive sprouting of noradrenergic sympathetic fibers in the axotomized sensory ganglia and the peripheral nerves.⁴⁻⁷

Stellate ganglion blockade (SGB) is not a totally benign procedure, as side effects include seizures, death, pneumothorax, paralysis of the recurrent laryngeal nerve, paralysis of the brachial plexus and an intravascular or subarachnoid injection. Furthermore, not all patients with CRPS I of the hands respond to this therapy. The purpose of this study, therefore, was to attempt to ascertain what patients, if any, may respond to SGB therapy.

In the present study, we evaluated the efficacy of stellate ganglion block therapy for the treatment of CRPS I of the hand in 25 patients who met the International Association for the Study of Pain (IASP) clinical criteria for CRPS:

Key Points

- An inverse relationship exists between hand perfusion and the duration of symptoms of type 1 complex regional pain syndrome.
- A positive correlation exists between stellate ganglion block efficacy and how soon stellate ganglion block therapy is initiated.
- A duration of symptoms greater than 16 weeks before the initial satellite ganglion block (SGB) and/or a 22% decrease in skin perfusion between the normal and affected hands adversely affects the efficacy of SGB therapy.

- 1) The presence of regional pain and sensory changes following a noxious event.
- 2) Pain associated with findings such as abnormal skin color, temperature change, abnormal sudomotor activity or edema.
- 3) No distribution of the pain of a single nerve in the extremity.
- 4) The combination of these findings exceeding their expected magnitude in response to known physical damage during and following the inciting event.⁸

Methods

This is a prospective clinical study. Twenty-five subjects, between 26 and 56 years of age with CRPS I following carpal tunnel release of one hand were randomly selected to be in this study following Institutional Review Board approval and patient signed informed consent. All 25 patients with CRPS I met the IASP criteria previously mentioned. Patients were included in this study whether or not they had relief following SGB therapy. It has been our experience that patients with CRPS I have the following responses to sympathetic blockade: 1) complete relief, 2) partial relief or 3) no relief. We therefore assigned patients in our study to one of these three groups for analysis.

Subjects were excluded from this study if they had a history of upper extremity cellulitis, Raynaud disease or Raynaud phenomena. No patient was included in this study if they used any medication or substance which could affect sympathetic function. No patient was included in this study unless they had a numeric pain intensity score (NPIS) ≥ 7 . Furthermore, no patient was included in this study unless they had an adequate SGB defined as: increased temperature of greater than 2°C in the affected hand, a Horner syndrome and a decrease in the pain in the affected hand. Each patient received SGB therapy once a week for a total of three injections using an anterior-lateral approach with fluoroscopy.⁹ SGB was done with 5 mL of 0.5% preservative-free lidocaine (Abbott Labs, N Chicago, IL). Each injection of local anesthetic was preceded by the administration of 2 mL of iohexol 300 (Isovue, Nycomed, Princeton, NJ) to ascertain proper needle placement as well as adequate vertical and caudal spread of the injectant.

Skin surface temperature was measured in both hands using an Omega Medical infrared continuous skin surface temperature scanner at the time of the initial evaluation and two weeks following the third SGB. Pain intensity scores were recorded two weeks following the last SGB and monthly for 6 months in this study. An NPIS (0-10) was used to record patient pain and analgesic responses, pre- and post-SGB. Pre- and postinjection Beck Depression Inventory scores (0-63) as well as Pain Disability Index scores (0-70) were obtained.

We examined basal and reflex-evoked changes in the skin blood flow with a Moor laser Doppler imaging (LDI,

Moor Instruments Inc., Wilmington, DE) at the initial evaluation and two weeks following the last SGB on both hands in a temperature-controlled room (20 - 23°C). The dorsum of both hands of each individual in this study was scanned from distal to proximal. A sampling time of 4 milliseconds/pixel was used. The distance from the laser beam to each hand was 50 cm. The term used to describe blood flow measured by the LDI technique in this study was 'flux': a quantity proportional to the product of the average speed of the blood cells and their number concentration (often referred to as blood volume). An inspiratory gasp against resistance (Mueller maneuver) was used to cause a short sympathetic stimulus response which has been shown previously to be accompanied by peripheral vasoconstriction.¹⁰⁻¹² The LDI was done with and without Mueller maneuver to assess the function of sympathetic nervous system in each individual. Beck Depression Inventory scores and Pain Disability Index scores were administered to all patients before the first stellate ganglion block and two weeks following their last SGB. Complete pain relief was defined as NPIS = 0. Partial relief was defined as NPIS <7, while no relief was defined as NPIS ≥ 7 . Data were expressed as mean \pm SD unless otherwise specified. Statistical analysis consisted of the paired Student's *t* test, the Pearson product-moment correlation, Kruskal-Wallis test and Dunn's multiple comparison tests. In all comparisons, a *p* value <0.05 was considered significant following the appropriate statistical test for the analysis of data. All patient data was encoded to prevent retrieval of subject identity.

Results

Patient data was reviewed without identifiers. Patient demographics are summarized in Table 1. Following SGB therapy, 10/25 (40%) patients in this study had complete pain relief following SGB, 9/25 (36%) had partial pain relief and 6/25 (24%) had no pain relief (Table 2). Laser Doppler flux differences between the affected hands and the normal hands with and without Mueller maneuver before and after SGB therapy demonstrated that there was a significant flux difference ($P < 0.05$) pre-SGB between the affected hand and the normal hand compared with Mueller maneuver, while post-SGB therapy demonstrated no significant flux difference between the affected and normal hands with Mueller maneuver, which suggests an improvement of sympathetic function post-SGB. The mean flux difference between the right and left hand baseline was 1.8 ± 0.98 , while the flux difference immediately following Mueller maneuver was 1.9 ± 0.9 , which was not statistically significant.

The patients who had a 22 ± 7 flux unit decrease in perfusion units before SGB therapy in their affected hand compared with their normal hand had no relief with SGB. The patients who had a decrease in perfusion of 11 ± 3 flux units had partial relief of their pain following SGB, while patients who had an increase in perfusion of the affected hand

Table 1. Demographics

Group	Age (yrs)	Gender	Hand dominance	Side of CRPS
I (n=10)	39 ± 47	6/10 (60%) female 4/10 (40 %) male	Right: 4/6 (67%) Right: 3/4 (75%)	Right: 5/6 (83%) Right: 3/4 (75 %)
II (n=9)	36 ± 5	5/9 (56%) female 4/9 (44%) male	Right: 4/5 (80%) Right: 3/4 (75%)	Right: 4/5 (80%) Right: 3/4 (75 %)
III (n=6)	37 ± 6	4/6 (67%) female 2/6 (33%) male	Right: 3/4 (75%) Right: 2/2 (100%)	Right: 3/4 (75%) Right: 2/2 (100%)

when compared with the normal hand had complete pain relief following SGB therapy. The mean duration between the onset of the CRPS I signs and symptoms and the first SGB was 14.7 ± 17.7 weeks, which ranged from 3 to 84 weeks. The difference of the skin temperature between the affected and unaffected hands averaged $2.30 \pm 0.07^\circ\text{C}$ pre-SGB, and $0.78 \pm 0.2^\circ\text{C}$ post-SGB ($P < 0.01$).

The decrease in the flux value in response to Mueller maneuver averaged $3.6 \pm 0.4\%$, ranging from 3.1 to 4.7% and $3.9 \pm 0.4\%$, ranging from 2.8 to 4.4% for the left and right hands, respectively. Abnormal flux values for the affected hands with CRPS I occurred in all 25 patients. Before Mueller maneuver, the mean differences (including both decreased or increased flux values on the affected limb) between unaffected and affected hands averaged $15 \pm 1.4\%$. Compared with the contralateral limb, 10/25 (40%) of the patients had increased flux values while 15/25 (60%) of individuals had decreased flux values.

Three clinical groups were identified in this study which was based on pain intensity results: group I—complete pain

relief, group II—partial pain relief and group III—no pain relief. Significant differences were noted between groups I and II and I and III ($P < 0.5$), with respect to the duration between the onset of symptoms until the initiation of therapy (Table 2). There were no differences in the pain intensity scores pre-SGB in the different groups. With reference to flux differences, patients in group I had an 8.9 ± 0.8 increase in flux units in the hands with CRPS compared with the normal hands while groups II and III had 7.3 ± 3.9 and 14.4 ± 6.3 flux units ($P < 0.5$ compared with groups I and II decreases) respectively. Following SGB therapy, the following difference in perfusion units were noted between the affected and normal hands: I: 1.2 ± 1.0 ; II: 3.0 ± 2.6 ; and III: 12.6 ± 3.4 ($P < 0.5$ compared with I and II). Patients who had a mean $22\% \pm 14$ perfusion unit decrease or greater in the hands with CRPS I compared with their normal hands had no relief with SGB therapy. The patients in groups II and III had a repeat series of SGB with no significant changes in pain intensity scores or blood flow perfusion units post-SGB.

The mean perfusion differences between the normal and

Table 2. Subgroup comparisons pre- and poststellate ganglion therapy

Subgroups	I (n = 10)	II (n = 9)	III (n = 6)
Time until SGB (wks)	4.6 ± 1.8 ($P < 0.05$ with II and III)	11.9 ± 1.6	35.8 ± 27
Flux pre-SGB	8.9 ± 3.9	-7.7 ± 4.0	-14.4 ± 6.3 ($P < 0.05$ with II and III)
Flux post-SGB	1.2 ± 1.0	-3.0 ± 2.6	-12.6 ± 3.4 ($P < 0.05$ with II and III)
NPIS pre-SGB (0–10)	8.7 ± 0.7	8.6 ± 0.7	8.8 ± 0.7
NPIS post SGB (0–10)	0 ($P < 0.05$ with II and III)	5.3 ± 0.9	8.8 ± 0.7
Duration of pain relief (wks)	29 wks (complete relief)	29 wks (partial relief)	0 weeks (no relief)
Depression score pre-SGB (0–63)	34 ± 8	27 ± 7	29 ± 9
Depression score post-SGB (0–63)	11 ± 9 ($P < 0.05$ with II and III)	19 ± 4	26 ± 7
Disability Index pre-SGB (0–70)	60 ± 8	59 ± 8	63 ± 5
Disability Index post-SGB (0–70)	14 ± 10 ($P < 0.05$ with II and III)	39 ± 13	58 ± 9

*Hand skin perfusion measurements are given in "flux" units.

SGB, stellate ganglion blockade; NPIS, numeric pain intensity score.

CRPS I hands progressed from increased perfusion to decreased perfusion as the duration of symptoms increased ($r = -0.82$) (Fig. 1). Patients who had early SGB treatment following the onset of their symptoms had significantly better pain relief following SGB therapy ($r = 0.9$).

Discussion

A comprehensive review of the use of SGB for the treatment of CRPS published in 2002 questioned the efficacy of this modality.¹³ However, the results of our study demonstrated that the clinical efficacy of SGB therapy is high when initiated within 12 weeks from the time of symptom onset. A placebo control was not used in this study, as placebo utilization was not permitted by our Institutional Review Board. As a result, there is a chance that some of the patients had a placebo response to SGB therapy. On the other hand, we feel that this is unlikely, due to the observation that differences in blood perfusion and skin surface temperatures were noted among the groups between normal hands and hands with CRPS I. We would not expect significant unilateral physiologic changes to be placebo related. However, decreases in pain reports could be placebo related. This is the reason that we chose to measure temperature and skin perfusion changes.

Clinical research has shown that nerve injury is often accompanied by dysfunction of the peripheral sympathetic nervous system which ultimately causes microcirculatory disturbances.¹⁴⁻¹⁹ The results from our study demonstrated that the majority of our CRPS I patients had impaired sympathetic reflex function, which is consistent with a previous report that autonomic abnormalities with skin vascular function occur in patients with CRPS I due to the disturbances of sympathetic innervations.²⁰ Our study results did indicate a decrease in sympathetic outflow at the initial onset of CRPS I as evidenced by increased hand blood flow correlating with an increase in sympathetic stimulation, with decreased blood flow over time. The specific reasons for these observations

Hand Perfusion Differences and Duration of Symptoms

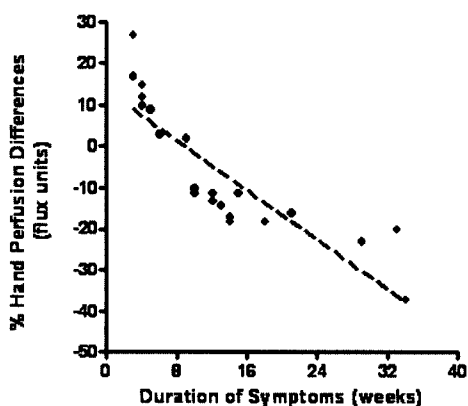


Fig. 1 Correlation of perfusion differences of the normal and CRPS I hands with the duration of symptoms ($r = -0.82$)

Post Injection NPIS

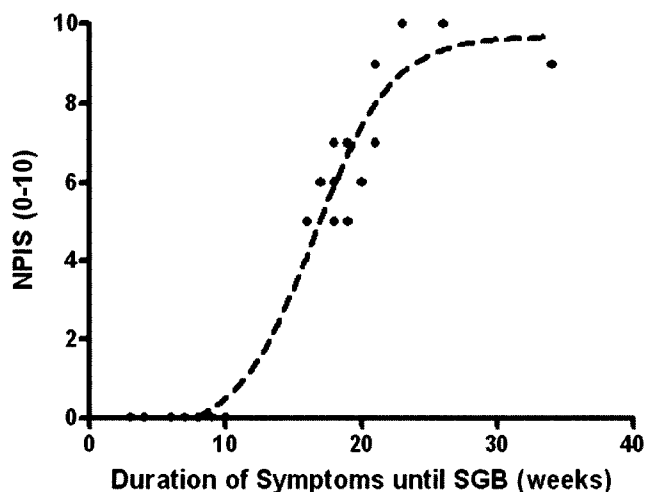


Fig. 2 Patients who had early SGB treatment had significantly lower Numeric Pain Intensity Scores following SGB therapy ($r = 0.9$).

remain to be elucidated, but may be explained by possible elevated calcitonin gene-related peptide (CGRP) levels in patients with acute CRPS. Elevated levels of CGRP suggest neurogenic-related acute inflammation with ensuing vasodilatation as a pathophysiologic mechanism contributing to early symptoms of CRPS I.²¹ Normalization of CGRP levels, on the other hand, has been shown to be accompanied by clinical improvement of local inflammatory signs in patients with CRPS.

The results of our study support the concept that three CRPS subgroups exist as previously described by Bruhl et al.²² We attribute the observed decrease in hand blood flow noted on LDI in our patient population to possible dorsal root ganglia (DRG) sympathetic fiber sprouting. Our hypothesis is supported by a laboratory study by Kim et al that used segmental nerve ligation as an experimental model for CRPS. Their study demonstrated extensive DRG sympathetic sprouting with the development of adrenergic sensitivity in the affected sensory nerves.²³ We chose lidocaine for our study because lidocaine administered topically on an injured nerve has been shown by Zhang et al to significantly decrease abnormal DRG sympathetic sprouting.²⁴ The results of our study do suggest that SGB therapy with lidocaine may decrease sympathetic sprouting in humans as well.

We conclude from our study results that both increased and decreased vasomotor activity can occur with CRPS I depending on the duration of the symptoms. We furthermore conclude that SGB therapy is more efficacious with decreased vasomotor activity but becomes less effective with increased vasoconstriction. The mixed SGB efficacy results of our study are related to both the duration of the symptoms and blood perfusion in the affected hands. In summary, we feel that the

early diagnosis and treatment of CRPS I should significantly improve patient outcome in the clinical setting.

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