Stellate ganglion block beyond chronic pain: A literature review on its application in painful and non-painful conditions

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Abstract

Cervical sympathetic or stellate ganglion blocks (SGBs) have been commonly used in the treatment of painful conditions like complex regional pain syndrome (CRPS). However, there is literature to suggest its utility in managing non-painful conditions as well. The focus of this literature review is to provide an overview of indications for SGB for painful and non-painful conditions. We identified published journal articles in the past 25 years from Embase and PubMed databases with the keywords "cervical sympathetic block, stellate ganglion blocks, cervical sympathetic chain, and cervical sympathetic trunk". A total of 1556 articles were obtained from a literature search among which 311 articles were reviewed. Among painful conditions, there is a lack of evidence in favor of or against the use of SGB for CRPS despite its common use. SGB can provide postoperative analgesia in selective surgeries and can be effective in temporary pain control of refractory angina and the acute phase of herpes zoster infection. Among non-painful conditions, SGB may have beneficial effects on the management of post-traumatic stress disorder (PTSD), refractory ventricular arrhythmias, hot flashes in postmenopausal women, and breast cancer–related lymphedema. Additionally, there have been various case reports illustrating the benefits of SGB in the management of cerebral vasospasm, upper limb erythromelalgia, thalamic and central post-stroke pain, palmar hyperhidrosis, orofacial pain, etc. In our review of literature, we found that SGB can be useful in the management of various non-painful conditions beyond the well-known treatment for CRPS, although further studies are required to prove its efficacy.

Keywords: Cervical sympathetic block, complex regional pain syndrome, stellate ganglion

Introduction

Cervical sympathetic blocks are frequently used in the management algorithm of complex regional pain syndrome (CRPS) for pain control. Autonomic disturbances have been implicated as one of the mechanisms leading to amplification and chronicity of pain in some of these conditions. Following injury and inflammation, the sprouting of sympathetic fibers in the dorsal root ganglion and adrenoceptor upregulation on nociceptors and keratinocytes lead to prolonged pain and hyperalgesia.[1,2] Hence, sympathetic blocks like stellate ganglion blocks (SGB) are used in the treatment of various conditions where sympathetic input is thought to play a role in their pathophysiology. Recent studies have indicated a larger and broader use for this modality in conditions ranging from post-traumatic stress disorder (PTSD), refractory arrhythmias, breast cancer–related complications, and cervical headaches. The focus of this narrative review is to provide an overview of the variety of indications for stellate ganglion blocks along with their contraindications.

Methods

We identified journal articles published in the past 25 years on Embase and PubMed databases with the keywords "cervical

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sympathetic block, stellate ganglion blocks, cervical sympathetic chain, and cervical sympathetic trunk". A total of 1556 articles were obtained from the literature search after the removal of 661 duplicates. Among these, 311 articles were selected for review. We summarized and organized textual data under each subheading based on the various indications the SGB was used for and we reported the principal findings [Table 1].

Review

Stellate ganglion blocks for painful conditions

Complex regional pain syndrome type - 1

CRPS is a chronic pain condition usually involving a limb that can present with varied symptomatology with persistent pain disproportionate to the magnitude of the inciting injury. The widely accepted International Association for the Study of Pain (IASP) diagnostic criteria based on symptoms and signs in categories of sensory, vasomotor, sudomotor, and motor changes have improved the specificity and sensitivity of diagnosing this condition.[3] The subtypes of CRPS are based on the existence (type 2) or lack (type 1) of a discrete nerve lesion. SGB allows for the disruption of the pain cycle by reducing sympathetic tone to prevent central sensitization in CRPS of the upper limb. SGB results in the enhanced range of movement of the affected limb, vasodilation, elevation in skin temperature, and improvement in pain.[4] CRPS can also be subdivided into sympathetically maintained (SM) versus sympathetically independent pain, which provides some explanation as to why certain patients do not receive adequate pain relief despite optimal nerve blockade.[4]

Ongoing pain in CRPS patients causes cortical reorganization, as demonstrated by cortical shrinkage in the primary somatosensory cortex.[5] In a small prospective case series in CRPS patients with sympathetically maintained pain, isolated SGB showed functional magnetic resonance imaging (fMRI) evidence of reversal of cortical shrinkage and increased blood oxygenation levels along with reduction of pain scales one hour following SGB.[6] This illustrates that sympathetic blockade leads to a reduction in pain afferents to the somatosensory cortex. The duration of the pain relief with sympathetic blockade lasts longer than the duration of action of the local anesthetic.[7] This has been the rationale for the incorporation of these blocks in the management algorithms of CRPS. However, the contribution of the sympathetic nervous system in the development of this syndrome and the efficacy of the sympathetic blocks in its management has been continuously debated. A systematic review published by the Cochrane Collaboration concluded that there was a lack of evidence to support or refute the use of local anesthetic sympathetic blockade in the pain management of CRPS.[8] This review included all types of sympathetic blocks including SGB, thoracic, and lumbar sympathetic blocks for management of CRPS. There were only two placebo-controlled studies in this review, both of which included SGBs in CRPS and there was no difference in the pain scores between the groups.[7,9] The duration of pain relief was longer with SGB (90 vs. 20 hours) in one study[7] and the edema, hand grip strength, and functional hand scale were better with SGB in the other study.[9] But the size of the studies was too small to derive any firm conclusions. Two studies investigated the effect of the addition of SGB to conservative management like physical therapy, pharmacotherapy, and rehabilitation.[10,11] One study ($n = 82$) showed improved therapeutic efficacy (defined as a proportion of a minimum of 50% reduction in pain) and reduced relapse of CRPS at two months following treatment with or without SGB in addition to physical therapy and pharmacotherapy.[10] The other study ($n = 60$) did not find any benefits of adding SGB to rehabilitation in shoulder-hand syndrome following stroke.[11] However, guidelines do suggest that if the sympathetic blocks provided good analgesia, a series of blocks can be advocated to bring forth a relatively painless window and an opportunity to facilitate active physiotherapy and rehabilitation.[12]

Postherpetic neuralgia (PHN)

Post-herpetic neuralgia (PHN) is a debilitating neuropathic pain that occurs following a painful rash due to shingles. A recently published clinical trial showed the beneficial effects of ultrasound-guided SGB in craniofacial post-herpetic neuralgia when combined with extracorporeal shockwave therapy.[13] A randomized trial investigated the effect of early SGB for acute herpes zoster of the face and showed that SGB significantly reduced the intensity of acute pain, and shortened its duration in addition to antiviral therapy. Patients who received SGB also had a significantly lower incidence of PHN (6.5% vs. 27% at three months and 0% vs. 13% at six months) when compared to the control group.[14] A systematic review and meta-analysis in 2017 concluded that application of SGB during the acute phase of herpes zoster shortened the duration of pain but did not reduce the incidence of PHN.[15]

Refractory angina

Refractory angina is long-lasting chest pain due to reversible ischemia from obstructive coronary artery disease unresponsive to multiple medical therapies and coronary revascularization techniques. Case reports and case series have identified a role of SGB in modulating sympathetic tone, as the innervation to the heart largely lies in the caudal cervical and first four thoracic segments.[16,17] In a prospective observational study, 227 SGBs were performed in 46 patients and 100 paravertebral blockades (PVB) were performed on 21 chronic refractory angina (CRA) patients. Thirty-one among

Table 1: Summary of key findings

Painful conditions	
Complex regional pain syndrome (CRPS)	Limited evidence does not support or refute the role of local anesthetic sympathetic blockade in the pain management of CRPS. A series of blocks can be advocated to provide a pain-free window to facilitate active physiotherapy and rehabilitation.
Post-herpetic neuralgia (PHN)	RCTs have shown that SGB during the acute phase of herpes zoster may shorten the duration of pain.
Refractory angina	Observational data suggest that SGB may provide temporary symptom relief with refractory angina.
Acute post-surgical pain	Limited evidence shows postoperative analgesic benefits of SGB in upper limb orthopedic procedures, unilateral mastectomies, and head and neck oncologic surgeries.
Non-painful conditions	
Post-traumatic stress disorder (PTSD)	RCTs and prospective studies have demonstrated that SGB reduced PTSD symptoms.
Refractory ventricular arrhythmias (VA) or electrical storms	Systematic reviews of case series have concluded that SGB was effective in the management of acute electrical storms.
Menopausal vasomotor symptoms	RCTs have shown that SGB reduces the frequency of moderate-to-very-severe VMS (hot flashes).
Breast cancer–related lymphedema (BCRL)	RCTs and systematic reviews suggest that SGB is effective in reducing swelling in breast cancer–related lymphedema.
Cerebral vasospasm	Observational data have shown that SGB may relieve the cerebral vasospasm after SAH but the data is limited to support its use in the high mortality condition.

46 patients (67%) who received SGB had at least a two-week duration of pain relief, with a mean of 3.8 weeks. The response rate with two weeks of pain relief in the patients who received PVB was 52% (11/21).[18] In another case report, a 55-year-old patient with refractory angina experienced six weeks of pain-free episodes following the first block. The second SGB at this point provided three months of pain relief and he had a total of nine SGBs every two to four months. Overall, there was an improvement in quality of life for the next two years and there were no hospital admissions for 30 months.[16] In a double-blinded, placebo-controlled study on 51 patients with refractory angina, SGB with 15 mL bupivacaine versus normal saline reduced the frequency of angina with no significant differences between them, suggesting a mechanism of analgesia being either placebo or mechanical.[19] Hence, further studies are needed to explore this technique for its utility in refractory angina, especially with the recent application of ultrasound guidance. Recently, stereotactic radiosurgical stellate ganglion ablation following a successful diagnostic SGB was reported to provide pain relief at one-year follow-up in a patient with refractory angina.[20]

Acute post-surgical pain

SGB was also used in multi-modal analgesia pathways postoperatively following upper limb trauma in orthopedic surgery in a small case series of four patients. Postoperatively, these patients received SGB and showed improvement in visual analog scale (VAS) scores and decreased consumption of morphine within the first 24 hours.[21] A randomized, controlled trial (RCT) comparing postoperative analgesic efficacy with preoperative SGB with local anesthetic in the upper limb orthopedic procedures showed a tramadol sparing effect and analgesic effect compared to the placebo control group.[22] The vasodilation from the sympathetic blockade leads to a washout of inflammatory mediators. Therefore, the modulation and attenuation of neuropathic pain are attributed as the reasons for resting analgesia. However, a randomized controlled trial comparing SGB perioperatively for arthroscopic shoulder surgery versus no SGB in a set of 46 patients did not find any difference between groups in postoperative pain management or analgesia within the first 48 hours.[23] Another group of investigators in a single-blinded, randomized study claimed that pre-incisional SGB effectively reduced acute postoperative pain in unilateral mastectomy.[24]

In a pilot study involving nine patients who underwent lateralized head and neck cancer surgery, preoperative SGB provided significant postoperative analgesia and an RCT is underway. They found that four out of nine patients did not require any narcotics during the postoperative period.[25]

Stellate ganglion blocks for non-painful conditions

PTSD

Post-traumatic stress disorder (PTSD) is a debilitating mental health disorder with pathological anxiety following a traumatic life event. Pharmacotherapy and psychotherapy are the mainstay of management in this condition. SGB was suggested as an adjuvant to the treatment for PTSD, based on initial success reported in case studies and series.[26,27] Rapid symptom relief and lack of stigma that is associated with the conventional treatments were notable advantages of this treatment. A large prospective case series involving 166 service members from military clinics demonstrated that a right-sided SGB reduced the PTSD symptoms by 70% persisting beyond 3 to 6 months.[28]

The first single-site pilot randomized trial investigating the effect of SGB and a sham procedure in 42 PTSD patients did not show any appreciable difference in the psychological or pain outcomes.[29] However, this study faced criticisms due to methodological flaws involving patient selection and randomization potentially influencing the results.[30] Subsequently, another multisite RCT comparing SGB to sham in 113 patients found that there was a clinically significant reduction in PTSD severity scores (CAPS-5) from −12.6 vs. −6.1 in the sham group (normal saline) after two SGBs were administered two weeks apart for over eight weeks. There was also an improvement in secondary outcome measures like depression, anxiety, mental and physical functioning, etc., when compared to the sham group.[31]

The mechanism of action of beneficial effects of SGB in PTSD is not well understood. It has been suggested that the SGB may reverse the neurobiological cascade triggered by trauma or stress that leads to the development of PTSD.[32] One hypothesis suggests that local anesthetic agents may improve PTSD, CRPS, and hot flashes by reversing the cascade of events that cause increased sympathetic sprouting, increased nerve growth factor (NGF), and an increase in the brain norepinephrine seen in these conditions. This hypothesis, called the unifying theory, provides a plausible explanation as to why the benefits of SGB extend beyond the duration of the action of local anesthetic.[33]

Refractory ventricular arrhythmias (RVAs)

The ventricular arrhythmias (VAs) can be often refractory to the standard anti-arrhythmic treatments. An electrical storm is described as ≥3 episodes of persistent ventricular tachycardia/arrhythmia within a 24-hour period and can be life-threatening. SGB has been used to interrupt the cardiac sympathetic activity which has a triggering and maintaining effect on VAs. SGB reduces sympathetic outflow to the myocardium and raises the threshold for VAs. It can be a useful treatment for refractory ventricular arrhythmias (RVAs) or bridge therapy before surgical sympathectomy. In animal myocardial infarction models, SGB has been shown to prolong duration of action potential, increase the refractory period while reducing transmural repolarization, and increase the ventricular fibrillation threshold.[34]

A systematic review that reviewed published studies from 1974 to 2016 included 38 patients from 23 studies—which were mostly case reports and series—and strongly concluded that SGB was effective in the management of acute electrical storms. The systematic review also noted an immediate decline in VA following SGB from 12 episodes per day to one per day ($P < 0.001$) and the number of shocks by ICD from 10 shocks per day to 0.05 per day ($P < 0.01$).[35] Another systematic review published around the same time collated data from 22 case reports/series including 35 patients. Unilateral or bilateral SGBs decreased the VA episodes from 16.5 events to 1.4 before and after the intervention and the defibrillations from 14.2 to 0.6. These beneficial effects were noted regardless of the cause of cardiomyopathy, ventricular rhythm, and contractility.[36] The same authors published a single-center observational study on 20 consecutive patients and noted similar beneficial effects with bilateral SGBs performed under ultrasound guidance.[37] Another retrospective study included 30 patients with RVAs who received either left or bilateral SGBs under fluoroscopy or ultrasound guidance and showed a 92% reduction in the VA episodes in the 72 hours following the intervention.[38] Both of these studies claimed the safety of the SGBs with no major complications. There are no randomized trials published to date that investigate the SGBs on VAs and electrical storms, and hence there is a need for these in the immediate future to establish the role of this procedure which could be of significant therapeutic utility.

Hot flashes

Hot flashes, flushes, and night sweats are categorized as vasomotor symptoms (VMS), which is a common phenomenon experienced by women transitioning through menopause. Hot flashes are sensations of extreme warmth and sweating involving the face and upper body and affect 75% of women.[39] Oral hormonal therapy is an effective treatment in alleviating these symptoms, reducing the frequency of these symptoms by 75%.[40] However, hormonal therapy may not be suitable for everyone due to concerns of side effects and personal preferences. SGB was proposed as a nonhormonal alternative to relieve these symptoms based on the findings from a case series involving six patients. With the initial SGB, all of these patients had two to five weeks of relief, and a second block provided additional relief ranging from 4 to 18 weeks, and the third block for 15–48 weeks.[41] Subsequently, there were more case studies and open-label studies on SGBs in women with hot flashes from natural menopause and breast cancer survivors with similar results.[42-44] There is only one RCT published to date that compares the effects of image-guided SGB versus sham injection with saline on the frequencies of VMS in postmenopausal women ($n = 40$). The frequency of moderate-to-very-severe VMS was reduced by 50% from baseline at four to six months in the SGB group compared to the saline injection group (event rate ratio, 0.50; 95% CI, 0.35–0.71; $P < 0.001$).[45] Also the intensity of VMS was 38% less in the SGB group compared to the saline group. Hence this trial provided further evidence of the efficacy of SGB for this condition. Another open-label randomized trial in 40 breast cancer survivors demonstrated that SGB was more efficacious than pregabalin in the management of hot flashes.[46] More trials of larger size are needed to advocate its use in routine practice.

Breast Cancer-related lymphedema

Breast cancer-related lymphedema (BCRL) is a fairly common sequela after treatment for breast cancer and affects about 21% of these women.[47] Disruption to the normal lymph flow with radiation therapy or surgery is the known reason, causing swelling in the breast, upper limb, or trunk. Complex decongestive therapy (CDT) is the usual treatment aimed at mobilization of fluid and swelling reduction by exercises, compression massage, bandages, skincare, etc. SGB was reported to help decrease the swelling in a report published in 1983.[48] There have been several studies supporting this finding to date of which most are case reports and retrospective studies.[49-51] The mechanism of action of SGB in this condition is not known. The venous dilation following the sympathetic blockade may facilitate lymphatic draining and there may also possibly be an immunomodulatory effect. In a retrospective matched cohort study on patients who had secondary lymphedema after breast cancer treatments, 30 patients who had SGB were matched with another 30 who underwent CDT. Though both treatments reduced the edema compared to the baseline, the patients who had SGB had a greater reduction in the upper arm circumference.[51] A systematic review that included case reports, retrospective studies, and RCTs, assessed the effect of sympathetic nerve blocks in lymphedema in a sum of 187 subjects and noted that sympathetic blocks reduced lymphedema—shown by reduced limb circumference—and also improved patient-reported outcomes like pain.[52] A randomized trial compared SGB and CDT in 38 patients with BCRL and found both treatment modalities to be effective in reducing the swelling, and there were no significant differences among the groups. Hence, SGB can be considered as an alternative treatment modality for BCRL.[53]

Cerebral vasospasm

Cerebral vasospasm is a known complication of subarachnoid hemorrhage (SAH) which can lead to cerebral ischemia and worse neurological outcomes. The use of SGB for neurological symptoms has been reported since 1936 and there have been several reports of its use in cerebral vasospasm.[54-57] In an experimental rat model of SAH, cerebral vasodilatory effects of cervical sympathectomy had favorable neurological outcomes by alleviating cerebral vasospasm.[58] In the largest retrospective study to date involving 37 patients with aneurysmal SAH, SGB decreased the cerebral blood flow velocity by 20% for over 24 hours. The cerebral blood flow velocity is inversely related to cerebral vasodilation and blood flow.[59] Despite the theoretical benefits of SGB on cerebral blood flow, there is a lack of strong scientific evidence to support its routine use in cerebral vasospastic states. In an attempt to perform a systematic review and elucidate the role of SGB in cerebral vascular tone, a group of researchers were unable to clarify the impact of SGB on SAH which is a condition with high mortality.[60]

Other uses

Most recently a meta-analysis concluded that SGB improved postoperative gastrointestinal function recovery in surgical patients who underwent general anesthetics.[61] Case reports have also identified a positive benefit from SGB in the treatment of upper limb erythromelalgia,[62] upper limb ischemia,[63,64] pain from vasculitis,[65] painful congenital venous malformations of the arm,[66] persistent hiccups,[67] thalamic pain,[68] central post-stroke pain,[69] abducens palsy,[70] palmar hyperhidrosis,[71] refractory migraine,[72] refractory tension headache[73] and various types of orofacial pain.[74,75]

Conclusion

SGBs have shown a variety of uses in the management of various conditions beyond the well-known treatment for CRPS. There is limited evidence to support or refute the efficacy of SGB in the pain management of CRPS. SGB may be beneficial in the acute phase of herpes zoster for pain control. It may provide temporary symptom relief with refractory angina. Early clinical evidence suggests a potentially useful role in postoperative pain management for selected surgeries. SGB may be beneficial in a variety of non-painful conditions such as PTSD, RVAs, menopausal hot flashes, breast cancer-related lymphedema, and cerebral vasospasm. Although further studies with larger sample sizes are required, SGB remains a viable alternative treatment for various conditions.

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Conflicts of interest

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