ISSN 2307-8960 (online)

World Journal of *Clinical Cases*

World J Clin Cases 2023 April 6; 11(10): 2123-2362

Published by Baishideng Publishing Group Inc

World Journal of
Clinical Cases

Contents

Thrice Monthly Volume 11 Number 10 April 6, 2023

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RESPONSIBLE EDITORS FOR THIS ISSUE

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NAME OF JOURNAL
World Journal of Clinical Cases

ISSN
ISSN 2307-8960 (online)

LAUNCH DATE
April 16, 2013

FREQUENCY
Thrice Monthly

EDITORS-IN-CHIEF
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https://www.wjgnet.com/2307-8960/editorialboard.htm

PUBLICATION DATE
April 6, 2023

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World J Clin Cases 2023 April 6; 11(10): 2160-2167

DOI: 10.12998/wjcc.v11.i10.2160

ISSN 2307-8960 (online)

MINIREVIEWS

Treatment of stellate ganglion block in diseases: Its role and application prospect

Jing-Jing Deng, Cai-Ling Zhang, Dian-Wen Liu, Tao Huang, Jian Xu, Qing-Yan Liu, Yue-Nong Zhang

Specialty type: Medicine, research and experimental

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): B
Grade C (Good): C
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Ait Addi R, Morocco; Shirini K, Iran

Received: November 14, 2022
Peer-review started: November 14, 2022
First decision: February 17, 2023
Revised: February 24, 2023
Accepted: March 14, 2023
Article in press: March 14, 2023
Published online: April 6, 2023

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Abstract

The stellate ganglion (SG), as a type of sympathetic ganglion, consists of the sixth and seventh cervical vertebrae and the first thoracic sympathetic ganglia. SG block (SGB) is a minimally invasive injection that aims to inject low-concentration local anesthetics to induce a broad sympathetic blocking effect near the SG. There have been no changes and progress in the clinical application of SGB since the 1830s due to several potential risks, including hematoma from blood vessel injury, hoarseness from recurrent laryngeal nerve injury, and cardiopulmonary arrest. The feasibility and safety of SGB have greatly improved since the appearance of ultrasound-guided SGB. In recent years, SGB has been widely applied in the field of non-anesthesiology sedation, with significant therapeutic effects on pain, immunological diseases, somnipathy, psychological disorders, arrhythmias, and endocrine diseases. The present study reviews the present application of SGB in clinical practice.

Key Words: Echocardiography; Pain; Immunological diseases; Somnipathy; Psychological disorders; Arrhythmias; Endocrine diseases

Core Tip: Several reviews in the literature have contributed to the therapeutic effect of stellate ganglion block (SGB). The present study reviews the anatomical structure and mechanism of SGB, the advantages of ultrasound localization, and the application of SGB in the treatment of painful diseases, immunological diseases, somnipathy, psychological diseases, arrhythmias, and endocrine diseases.

Citation: Deng JJ, Zhang CL, Liu DW, Huang T, Xu J, Liu QY, Zhang YN. Treatment of stellate ganglion block in diseases: Its role and application prospect. *World J Clin Cases* 2023; 11(10): 2160-2167

URL: https://www.wjgnet.com/2307-8960/full/v11/i10/2160.htm

DOI: https://dx.doi.org/10.12998/wjcc.v11.i10.2160

INTRODUCTION

Development of the stellate ganglion block

Stellate ganglion block (SGB) has been applied in clinical practice for nearly a century to relieve pain-related syndromes, and treat vascular defects of the upper extremities. Since the 1940s, SGB has been performed to treat sympathetic pain conditions[1]. Over these years, through further exploration and investigation, the technique of blocking the cervical sympathetic nerve has been gradually established as a clinical treatment for certain diseases.

Anatomy of the stellate ganglion and stellate ganglion block

The stellate ganglion (SG), which is also known as the cervical and thoracic sympathetic ganglion, is a part of the cervical sympathetic trunk. The SG consists of the sixth (C6) and seventh (C7) cervical vertebrae, and the first thoracic sympathetic ganglia, which lies in front of the first costal neck, and extends to the inferior of the transverse process of C7. The preganglionic fiber of the SG crosses over the sympathetic chain of the neck, and the postganglionic fiber locates in the medial of the scalenus, outside of the longus cervicalis, esophagus and trachea, and the anterior aspect of the transverse process[2]. The SG provides sympathetic inputs to the ipsilateral upper limbs, chest, face and head. SGB aims to inject low-concentration local anesthetics near the SG, which can reversibly block the preganglionic and postganglionic fibers, and innervated area. Furthermore, SGB blocks the sympathetic nerves in the head, neck and upper limbs by acting on both pre-and post-ganglionic fibers[3]. The SGB procedure is described, as follows:

Before the procedure, patients who underwent SGB were instructed to relax and take the supine position, and the patient's neck was extended. Then, local anesthetics were injected between C6 and C7 to the surface of the long muscle of the neck, and the syringe was pulled out. The duration of the whole procedure was not more than 30 min. The success of the SGB was based on the following: Appearance of Horner's syndrome, elevated facial temperature, eardrum congestion, and nasal congestion. The efficacy of the SGB was traditionally evaluated by the emergence of Horner's findings, which included unilateral pupil reduction, ptosis, and the absence of sweat on the face. The perfusion index (PI) is the ratio of pulsating and non-pulsating signals. This was automatically and non-invasively measured to assess the pulse oxygen saturation. The use of the PI in regional anesthesia can improve the success rate of SGB, because this is a rapid, non-invasive and simple method that can provide early measurable data, when compared to Horner's sign and other similar clinical signs[4,5]. Therefore, the PI can be used as an indicator to evaluate the therapeutic efficacy of SGB. Previous studies have revealed that ultrasound-guided SGB can increase blood flow and reduce the vascular resistance of the arm. The decrease in vascular resistance and increase in blood flow of the arm may be significant indicators for a successful SGB. Thus, pulsed-wave Doppler can be used to monitor the success of SGB[6]. Doytchinova *et al*[7] reported that the sympathetic nerve activity of the skin can reflect the sympathetic nerve activity emitted by the SG, and that the sympathetic nerve activity on the skin surface can be measured by high-filtered electrocardiography. Compared to the subjective judgment of Horner's syndrome, the PI and cutaneous sympathetic nerve activity are more objective indicators to assess the success of SGB, which are presently hot research topics. However, the presence of Horner's syndrome is still more commonly used as an indicator of success of SGB in clinical practice.

Mechanism of the stellate ganglion block

SGB inhibits cardiovascular movement, glandular secretion, muscle tension, bronchial contraction, and pain conduction innervated by sympathetic nerve fibers from the SG distribution area. These can be taken as an advantage when treating some relative diseases involved in the head, neck, upper limb, shoulder and heart. The SG has extensive connections to the cerebral cortex, hypothalamus, amygdala and hippocampus[8]. Furthermore, SGB can regulate the autonomic nervous system, cardiovascular system, endocrine system, and immune system through the hypothalamic mechanism.

Ultrasound-guided stellate ganglion block

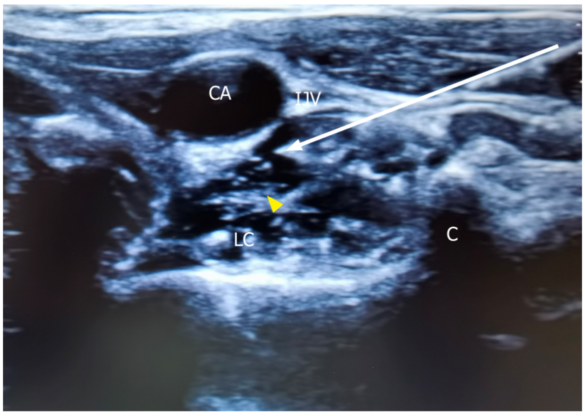
The SG is small in size, has a complex anatomical location, is adjacent to several important organs, and has more vessels and nerves. In addition, there is a certain proportion of anatomical variation in the population. Blind puncture of the SGB may easily lead to several severe complications, including hematoma caused by blood vessel injury and hoarseness caused by laryngeal recurrent nerve injury, which may lead to permanent Horner's syndrome. With the development of visualization technology, the positioning technology for SGB guided by X-ray, computed tomography, or ultrasound has become more accurate, greatly reducing complications. Compared to blind puncture, ultrasound-guided SGB greatly reduces the risk of SG puncture, and improves the success rate of the puncture. To date, ultrasound guidance has become the preferred method for SGB, when compared to blind and fluoroscopic guidance. The ideal position of the puncture during ultrasound-guided SGB should be anterolateral to the longus cervical muscle, and extend to the prevertebral fascia (in order to prevent diffusion along the carotid sheath), but should be shallow to the fascia that covers the longus cervical muscle (in order to prevent the injection of muscle material) (Figure 1). Thus, ultrasound-guided SGB improves the quality of the block, and requires fewer local anesthetics, when compared to traditional blind techniques [9]. In addition, ultrasound-guided SGB can improve surgical safety by allowing for the direct observation of vascular structures (inferior thyroid artery, common carotid artery, internal jugular vein) and soft tissue (thyroid, esophagus and nerve roots). The success rate of ultrasound-guided SGB can presently reach as high as 98%, and this can successfully prevent the involvement of the common carotid artery, internal jugular vein, and vagus nerve[10]. Therefore, ultrasound-guided SGB technology is bound to be rapidly popularized.

Stellate ganglion block and pain disorders

Although the mechanism of pain remains unclear, the application of SGB in the treatment of various types of pain remains feasible. Studies have revealed that the application of SGB to alleviate most of the symptoms of migraine in the treatment of migraine[11,12] and cluster headache[13] may be attributed to the inhibition of sympathetic overactivity or weakening of vascular inflammatory response. Furthermore, a previous study reported that ultrasound-guided SGB can effectively relieve cervical headache[14]. A successful case of SGB in the treatment of refractory tension headache was reported in 2019[15]. Furthermore, early SGB combined with antiviral drugs is a very effective treatment approach for herpes zoster or postherpetic neuralgia in the head, face and neck[16,17]. This significantly reduced the intensity and duration of acute pain, and reduced the incidence of postherpetic neuralgia. The therapeutic mechanism of SGB may be involved in improving the blood supply to the head and neck, inhibiting the hyperexcitability of sympathetic nerves, and reducing the synthesis and release of vasoconstricting substances, such as nitric oxide and prostaglandin. Similar cases on the treatment of SGB have also been reported for postoperative pain in head and neck cancer[18], peripheral arterial pain (Raynaud's disease[19], Burger's disease, diabetic vascular disease, arterial embolism, *etc.*), and neoplastic pain (pain after breast cancer resection)[20,21]. In pathophysiology, a part of the complex regional pain syndrome (CRPS) is considered to be correlated to autonomic disorders in the affected limb and the overreaction to catecholamines, which can lead to pain. SGB has been traditionally regarded as an important means for the diagnosis and treatment of CRPS-type I and -type II[22]. In the fourth edition of the American guidelines for the diagnosis and treatment of CRPS, the sympathetic block represented by SGB is listed as the first-line diagnosis and treatment. In a review of the results for CRPS, interventional pain physicians often performed SGB to relieve pain in the upper extremity of CRPS patients[23]. Therefore, SGB can be used as an effective treatment for pain diseases, which may provide underestimated clinical results.

Stellate ganglion block and Immune diseases

The immune system is the main defender of the body, and is involved in regulating the stability of the internal environment. The neurotransmitter released from the nerve terminus can diffuse and act on immune cells. For example, norepinephrine (NE) suppresses the immune response, acetylcholine and enkephalin enhances the immune response, and beta-endorphin sometimes promotes or suppresses the immune response. Furthermore, nerves can produce immune factors in certain circumstances. SGB can inhibit hyperactive sympathetic nerve activity, reduce levels of catecholamine and cortisol, weaken the stress response of the body, promote the recovery of human immune function, and further inhibit inflammation. A study[24] reported that ultrasound-guided SGB reduced the fluctuation of circulation, the concentration of peripheral adrenaline and cortisol, and the postoperative gastrointestinal dysfunction and stress response of patients who underwent radical resection of colorectal cancer. In addition, the anxiety during the perioperative period was relieved, and the recovery of gastrointestinal function after the operation was promoted. Furthermore, SGB can improve splenic $CD4^+$ T cell function after hemorrhagic shock, indicating its therapeutic effect on immunological diseases[25]. By blocking the sympathetic nerves that innervate the gastrointestinal system, SGB can expand gastrointestinal vessels, increase the blood supply, enhance gastrointestinal motility, and significantly relieve the symptoms of chronic ulcerative colitis[26].



DOI: 10.12998/wjcc.v11.i10.2160

Figure 1 Ultrasound-guided stellate ganglion block at cervical 6 Level. CA: Carotid artery; LC: Longus colli; IJV: Vena jugularis interna; C: Cervical 6 anterior tubercle of the transverse process; Yellow triangle: Stellate ganglion; White arrow: Needle for piercing.

Stellate ganglion block and sleep disorders

Somnipathy is closely correlated to melatonin, which is periodically secreted by the pineal gland throughout the day and night, affecting the body's sleep and awakening. In a study on sleep deprivation in rats with SGB, right SGB improved the dysfunction of spatial learning and memory in sleep-deprived rats. The mechanism may be attributed to the reduction in hippocampal apoptosis and inflammation in sleep deprived rats. Sleep deprivation is associated with decreased cognitive function mediated by melatonin, which inhibits the hypothalamic-pituitary-gonadal axis, reduces gonadotropin-releasing hormone levels, and reduces the levels of androgens, estrogens and progesterone by directly acting on the gonads. The various effects of SGB may exhibit similar effects on the therapeutic intervention mediated by melatonin[27]. A report on the application of SGB in a patient with excessive daytime sleepiness (EDS) revealed[28] that SGB produced obvious and desirable effects on EDS, which may be attributed to the stabilization of the autonomic nervous system by reversing the imbalance of the autonomic nervous system. Somnipathy is generally treated with drugs in clinical practice, which has certain disadvantages. Therefore, SGB treatment can be applied as an alternative treatment for patients.

Stellate ganglion block and psychological diseases

At present, more treatments, such as drugs and psychotherapy, are being performed for psychological diseases. However, there are still some difficulties. Therefore, more therapeutic measures are urgently needed to make up for the shortage. Kerzner *et al*[29] were the first to present a case on SGB in the treatment of depression in 1947 through a systematic review of prospects for clinical research on SGB for psychiatric disorders. These authors noted that the SGB improved the mood and occasional feelings of euphoria of the patients. In addition, the first case reported on the treatment of posttraumatic stress disorder (PTSD) by SGB in 1990 entailed the application of SGB in the treatment of a 15-year-old female with reflex sympathetic dystrophy and PTSD. SGB reduced the pain, and significantly improved the PTSD-related symptoms. These early studies are crucial, because these paves the way for subsequent researches on SGB as a treatment approach for mental illness. PTSD is defined by the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) as pathological trauma and stress disorders that occur in individuals following severe trauma. The lifetime prevalence of PTSD is approximately 3.9%. There are four types of symptoms: Re-experiencing the traumatic event, avoidance, persistent negative thoughts or feelings, and arousal and response associated with trauma[30]. In a multicentre randomized clinical trial of SGB for the treatment of PTSD[31], the incidence for active-duty military personnel with PTSD significantly decreased after eight weeks of SGB treatment. Therefore, SGB has been used to treat this disorder, providing long-term relief of sympathetic overactivity, and relieving the anxiety symptoms associated with PTSD.

Stellate ganglion block and arrhythmias

For the treatment of ventricular arrhythmias (VAs; such as congenital long QT syndrome, catecholamine-dependent polymorphous ventricular tachycardia, atrial fibrillation, and sinus tachycardia) and ischemic cardiomyopathy, SGB has frequently been taken as an adjuvant therapy. However, this is only carefully selected when adverse drug reactions could not be tolerated by the patient[32]. Refractory VAs are often exacerbated by increased sympathetic nerve tone in patients. Multiple studies[33-37] have revealed that SGB is associated with the dramatic decrease in VA burden, and these studies strongly recommend the use of SGB in refractory VA, offering potential promise for its wider use in high-risk populations. A randomized controlled trial observed the effect of SGB treatment to perioperative atrial fibrillation in patients undergoing lobectomy before surgery, and the results revealed that right SGB before surgery can significantly reduce the incidence of intraoperative and postoperative atrial fibrillation[38]. Furthermore, in a case where a patient with myocardial infarction failed to recover the autonomic rhythm after cardiopulmonary resuscitation in a hospital, the autonomic rhythm was recovered, and sufficient neural activity and hemodynamic recovery were observed after using SGB[39]. This may have been due to the inhibition of the release of NE, reduction in content of catecholamine, prolonged atrial effective refractory period, and increased in stability of cardiac electrophysiology induced by SGB. In addition, SGB can restrain the stress reaction, reduce the production of inflammatory markers, expand the blood flow of the coronary artery, and improve the oxygen supply of cardiomyocytes. Therefore, SGB, as the ending treatment for arrhythmia, provides a basis for the treatment of patients with malignant arrhythmia.

Stellate ganglion block and endocrine diseases

The nervous system is closely correlated to the endocrine system, and the extension of sympathetic nerve tension can affect the secretion of various endocrine glands. SGB can reverse the autonomic imbalance caused by the increase in sympathetic tone, and affect the neuroendocrine system. Vasomotor symptoms (VMS), which are also known as hot flashes and night sweats, are common symptoms of menopause. These are associated with reduced quality of life in perimenopausal and postmenopausal women. SGB is a safe and effective treatment for women who are unable to use or choose not to use hormone therapy. Furthermore, SGB reduces and lengthens the nerve growth factor (NGF), and reduces the synthesis and release of NE in the brain, and content of NGF in the brain, thereby alleviating the hot flashes, CRPS and PTSD symptoms. Moreover, SGB inhibits the secretion of sweat glands and regulates body temperature, thereby alleviating symptoms. Rahimzadeh *et al*[40] reported that SGB is as effective as paroxetine in reducing the frequency of hot flashes in breast cancer survivors, and improving sleep quality, with minimal side effects and acceptable tolerance in patients. Several clinical cases have also reported that SGB can be used to treat hyperhidrosis, and the mechanism was considered to be mainly correlated to the decrease in sweating function due to the vasodilation and sympathetic nerve block in the dominant part of the SG[41]. Lee *et al*[42] also support the use of SGB for VMS in perimenopausal and postmenopausal women, especially for patients with severe symptoms and difficulty in receiving more conservative treatment.

The occurrence of diabetes mellitus (DM) is not only correlated to primary insulin dysfunction and metabolic syndrome, but also correlated to mental stress, dietary factors, and other factors that reduce insulin secretion, and/or increase the secretion of glucagon and other glucose-raising hormones through the neuroendocrine system. Diabetic cardiovascular autonomic neuropathy (DCAN) is a common complication of type 1 and type 2 DM, with high morbidity and mortality. SG neurons are usually surrounded by satellite glial cells (SGC). Axotomy, inflammation, and other injuries can activate SGC in the primary sensory ganglia. The P2Y12 receptor is expressed in SGC, and may be involved in the bidirectional communication with neuron-glial cells. Furthermore, the P2Y12 receptor may play an important role in the occurrence of diabetic cardiovascular complications, while the P2Y12 receptor in the SG plays a crucial role in DCAN. SGB can significantly improve the autonomic nervous regulation function in diabetic patients[43]. Furthermore, it has also been shown that SGB can reduce inflammation and improve nerve function during ischemic stroke in diabetic rats[44]. Therefore, SGB can increase perioperative safety, and reduce the risk of cardiac events in patients with type 2 DM.

Stellate ganglion block and refractory diseases

Medically unexplained symptoms (MUS) are defined as somatic symptoms that cannot be reasonably explained by any organic disease. A patient with MUS would have a good therapeutic effect after SGB [45], suggesting that repeated SGB may be effective for modulating nerves and reducing sympathetic activity. When Xu and Zhang[46] performed SGB on a patient who suffered from hypothyroidism, Hashimoto's encephalopathy, cerebral infarction, and frequent premature ventricular beats, the patient presented with significantly improved sleep quality and a restored sinus rhythm after treatment. This may be correlated to the improvement in central and peripheral nerve functions induced by SGB, which maintains the body's autonomic nervous activity, endocrine potency, and immune function. After recovering from coronavirus disease 2019 (COVID-19), a large proportion of symptomatic and asymptomatic patients would develop long-term COVID syndromes, which are also known as the acute sequelae of severe acute respiratory syndrome coronavirus 2 infection. According to the clinical case definition of the World Health Organization, long-term COVID-19 symptoms may include fatigue, orthostatic intolerance, rapid resting heart rate, shortness of breath, brain fog, sleep disturbances, fever, gastrointestinal symptoms, loss of smell, taste disorders, anxiety, and depression. In a latest medical report[47], long-term COVID-19 symptoms, including taste, smell and fatigue, were significantly improved in two patients after planetary ganglion block. This may be due to the involvement of SGB in the central sympathetic nerve adjustment, which increases cerebral blood flow, and re-balances the interaction between the nervous system and immune system. Therefore, SGB can be considered when conventional treatment is ineffective, or when there is no better treatment plan.

CONCLUSION

The present review reported the clinical application of SGB in the field of pain disease, autoimmune disease, somnipathy, psychological disease, arrhythmia and endocrine diseases, which is minimally invasive, and can easily be accepted by patients. This can provide an effective treatment plan for disease treatment, which is not widely recognized by relevant specialists at present. Therefore, it was considered that SGB has a broad application prospect, and that it is necessary to carry out more multidisciplinary cooperation to promote the use of SGB. The mechanism of action of SGB needs to be further studied for its application to a wider range of fields, providing more theoretical bases for its safety and effectiveness.

FOOTNOTES

Author contributions: Deng JJ and Zhang CL composed the manuscript; Liu DW and Huang T collected and sorted out the literature; Xu J and Liu QY edited and polished the manuscript; Zhang YN designed the outline and edited the manuscript; All authors have read and approved the final manuscript.

Conflict-of-interest statement: All the authors report no relevant conflicts of interest for this article.

Country/Territory of origin: China

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S-Editor: Li L
L-Editor: A
P-Editor: Li L

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