Stellate Ganglion Block for the treatment of olfactory and gustatory dysfunction in patients with Long COVID: Case Series

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Abstract

Weeks or months after recovering from COVID-19, a significant number of people are still experiencing fatigue, ‘brain fog’, headaches, cognitive impairment, smell or taste disturbances, myalgia and one or more other symptoms. This condition has been termed as Long COVID and dysautonomia is thought to play one of the important roles in the pathophysiology of this condition. The stellate ganglion block (SGB) is thought to restore autonomic nervous system functioning by temporarily inhibiting cervical sympathetic activity and is under investigation as a potential option for the treatment of persistent olfactory and gustatory dysfunction, headache and other symptoms of Long COVID. In this case series, we report that by performing SGB, we successfully treated and improved the quality of life of two patients with a Long COVID diagnosis who presented us with complaints of smell and taste sensory impairment.

Key points

- Fatigue, ‘brain fog’, headache, cognitive impairment, sleep, mood, smell or taste disturbances, myalgias, sensorimotor deficits and dysautonomia are the most frequently reported neurological symptoms of ‘Long COVID’.
- There are a few reports of using stellate ganglion block (SGB) to treat Long COVID symptoms and olfactory dysfunction of various etiologies.
- The chronic hypersensitivity of the sympathetic nervous system in patients with a Long COVID makes SGB a rational therapeutic option that directly targets the sympathetic nervous system.
- Recovery of olfactory and gustatory dysfunction at two-month follow-up, in our cases we observed 90% recovery in the first patient and around 40% recovery in the second patient.
- The fact that significant improvement in all other symptoms, such as impaired concentration, sleep disturbance, fatigue and myalgia, was observed shortly after SGB may provide a basis for the important role of dysautonomia in the pathophysiology of Long COVID cases.

Introduction

SARS-CoV-2 infection (COVID-19) has caused a major pandemic, with significant mortality and morbidity worldwide. Around 80% of patients experienced mild to moderate illness and 5% of those with severe disease developed critical illness [1]. It generally takes 7-10 days after the onset of symptoms to recover from mild SARS-CoV-2 infection and 3-6 weeks for severe/critical illness [2]. However, long-term follow-up of patients recovering from COVID-19 has shown that one or more symptoms persist in a significant percentage of people even weeks or months after COVID-19 [3-5]. ‘Long COVID’ or ‘Post-COVID-19 condition’ is a term used to describe the presence of a variety of symptoms even weeks or months after recovering from SARS-CoV-2, regardless of viral status [6]. ‘Long COVID’ is characterized as a disorder with a broad spectrum of clinical
manifestations that may be indicative of underlying pulmonary, cardiovascular, endocrine, hematological, renal, gastrointestinal, dermatological, immunological, psychiatric or neurological disease manifestations. The most common neurological symptoms of 'Long COVID' include fatigue, 'brain fog', headache, cognitive impairment, sleep, mood, smell or taste disturbances, myalgias, sensorimotor deficits and dysautonomia [7]. In COVID-19, dysautonomia, or more specifically increased sympathetic activity, can have adverse effects on pulmonary, cardiovascular, renal, metabolic, immune and neuroinflammatory homeostasis [7, 8].

Although the complete mechanism of action is unclear, there are some reports on the use of stellate ganglion block (SGB) for the treatment of Long COVID symptoms and olfactory dysfunctions with different etiologies [9-11]. The inferior cervical and first thoracic ganglia are fused in 80% of the human population and form the stellate ganglion. Injection of local anesthetic close to the stellate ganglion can block the activity of the entire cervical sympathetic chain.

In this case series, we report the positive clinical results we observed after stellate ganglion block in Long COVID patients who presented to our clinic with complaints of olfactory and gustatory disorders.

Case Reports

Case 1. A 27-year-old female patient was admitted to our clinic with complaints of cacosmia, cacogeusia, fatigue, impaired concentration, sleep disturbance, muscle pain and headache. 9 months ago, she had a moderate COVID-19 without hospitalization and the above complaints had persisted after her recovery. She had lost 7 kilograms during this period. She was examined in Neurology and Otorhinolaryngology departments and diagnosed with 'Long COVID'. The patient underwent olfactory training and was prescribed corticosteroids and duloxetine. She did not benefit from the recommended treatments.

The patient is a non-smoker and has no other systemic comorbidities. The magnetic resonance imaging (MRI) scan of the head and brain displayed results consistent with normal anatomical and functional characteristics.

The patient was informed in detail about the procedure and that the data could be used for scientific purposes and, a consent form was obtained. She underwent right-sided SGB under ultrasonography guidance using 6 ml solution containing bupivacaine (15mg) and triamcinolone (10mg). Following the procedure, Horner’s syndrome developed on the right side. The patient, who came to the control a day after the procedure, stated that his complaints improved on the right side and she could taste coffee and chocolate, but her complaints continued on the left side. 48 hours after the first procedure, left-sided stellate ganglion block was performed with the same technique.

Before and after the SGB procedure, the patient was asked to rate severity of her complaints on a scale of 0 to 10 using the numerical rating scale (NRS). A score of 0 indicated that she had no complaints, whereas a score of 10 indicated that her complaints were intolerable. The patient was called for 2 follow-up examinations 1 week and 2 months after the procedure and evaluations were performed.

At both follow-up examinations, the patient reported a significant reduction in complaints and an improved quality of life. The results of the patient’s evaluation can be seen in more detail in Table 1 below.

<table>
<thead>
<tr>
<th></th>
<th>Pre-procedure assessment</th>
<th>1 week after the procedure</th>
<th>2 months after the procedure</th>
<th>Achieved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cacosmia</td>
<td>10</td>
<td>1</td>
<td>1</td>
<td>90</td>
</tr>
<tr>
<td>Cacogeusia</td>
<td>10</td>
<td>1</td>
<td>1</td>
<td>90</td>
</tr>
<tr>
<td>Fatigue</td>
<td>7</td>
<td>0</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>Impaired concentration</td>
<td>8</td>
<td>1</td>
<td>1</td>
<td>87,5</td>
</tr>
<tr>
<td>Sleep disturbance</td>
<td>6</td>
<td>2</td>
<td>1</td>
<td>83,3</td>
</tr>
<tr>
<td>Myalgia</td>
<td>7</td>
<td>3</td>
<td>2</td>
<td>71,4</td>
</tr>
<tr>
<td>Headache</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>100</td>
</tr>
</tbody>
</table>

Table 1. Assessment of the severity of complaints with numerical rating scale (NRS [0-10]) before and after the procedure – Case 1
Case 2. A 24-year-old female patient was presented to our clinic with complaints of anosmia, ageusia, myalgia and headache. She had 2 incidences of COVID-19 8 months apart, both of which were mild. Although anosmia and ageusia resolved after 3 months after her first illness, her complaints persisted for last 6 months despite recovery from her second illness. The patient was previously examined in the Neurology department and her complaints were linked to Long COVID. Olfactory training was recommended and applied for the last 2 months, but she reported no benefit. She was referred to us for SGB.

The patient reported no problems with the senses of taste and smell before undergoing COVID-19. She is a non-smoker and has no systemic comorbidities. Her magnetic resonance imaging (MRI) evaluation of the head and brain exhibited a standard anatomical and functional profile.

She was given detailed information about the SGB and that the data could be used for scientific purposes and, approval for the procedure was obtained. The patient underwent right-sided stellate ganglion block first and then 48 hours later left-sided stellate ganglion block using 6 ml solution containing bupivacaine (15mg) and triamcinolone (10mg) under ultrasonography guidance. Following each intervention, Horner’s syndrome developed on the involved side. At the 1-week follow-up examination, although the severity of the complaints decreased, the patient thought that it was not enough and the right and left SGB were applied again at 48 hours intervals with the technique described above. The patient was called for a follow-up appointment at the end of the 1st week and 2nd month after the last procedure. She reported no significant improvement after the second procedure, but continued decline from the first bilateral procedure and an improvement in quality of life. When she was informed that the procedure could be repeated, she reported that her current condition was satisfactory and that she did not wish to undergo further procedures.

The severity of the complaints was evaluated with the scale we described in the first case. The results of the patient’s evaluation can be seen in more detail in Table 2 below.

<table>
<thead>
<tr>
<th></th>
<th>Pre-procedure assessment</th>
<th>1 week after the 1st procedure</th>
<th>1 week after the 2nd procedure</th>
<th>2 months after 2nd procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anosmia</td>
<td>8</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Ageusia</td>
<td>7</td>
<td>4</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Myalgia</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Headache</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 2. Assessment of the severity of complaints with numerical rating scale (NRS [0-10]) before and after the procedure – Case 2

Discussion

In this case series, we report that patients who presented to our clinic with olfactory and gustatory dysfunction and other symptoms associated with Long COVID improved after stellate ganglion block. This improvement suggests that the regional sympathetic system is involved in the process in Long COVID patients and that in some patients the dysautonomy theory is relevant to the pathophysiology of the disease.

The SARS-CoV-2 virus has an RNA strain as genetic material and includes three protein structures: spike, envelope and membrane. The spike binds to the Angiotensin Converting Enzyme 2 receptor (ACE2) [12]. In accordance with the regional distribution of ACE2 receptors in the CNS, numerous neurological symptoms encountered in Long COVID patients, including hyposmia, mood disorders, cognitive impairment, sleep disturbances and dysautonomia, have been associated with dysfunction of ‘ACE2-rich’ brain regions [13]. SARS-CoV-2 entry through the olfactory epithelium and increased expression of ACE2 and TMPRSS2 (Transmembrane Serine Protease 2) facilitate neurotropism of the virus and subsequent dysautonomia in long COVID patients. The persistent olfactory dysfunction observed in Long COVID patients may be related to a cascade of effects generated by dysautonomia leading to ACE2 antibodies that enhance a persistent immune activation [14, 15]. A study by E. Guedj et al. [16] shows a profile of brain PET hypometabolism in patients with Long COVID, involving the olfactory gyrus and associated limbic/paralimbic regions and extending to the brainstem and cerebellum. Chronic sympathetic hypersensitivity in patients with long COVID makes
SGB a reasonable treatment modality that directly targets the sympathetic system. SGB increases both cerebral and regional blood flow and can restore autonomic nervous system function.

The stellate ganglion is a structure 1 to 2.5 cm long, about 1 cm wide and 0.5 cm thick. It is found in approximately 80% of the population and is formed by the fusion of the inferior cervical ganglion and the first thoracic ganglion [17]. All sympathetic flow to the head and neck structures either synapses in the stellate ganglia or goes via the more cephalic sympathetic ganglia. Therefore, stellate ganglion block is a complete sympathetic denervation of the head and neck [18, 19]. Stellate ganglion block is a common intervention in the diagnosis and treatment of sympathetic-induced pain and vascular insufficiency of the upper extremities. Furthermore, this type of block is recommended for the treatment of various medical conditions such as phantom pain, cancer pain, cardiac arrhythmias, postherpetic neuralgia, and orofacial pain [19].

Generally, SGB is not performed bilaterally because it may cause airway compromise due to bilateral recurrent laryngeal nerve palsy and respiratory compromise due to bilateral phrenic nerve palsy [20]. The optimal time interval between right and left SGB performed for long COVID is not known, and it is reported in the literature as 24 hours, 72 hours and 12 days [9-11]. Based on our previous clinical experience with SGB, we administered it 48 hours apart in both patients.

There are few case reports in the literature of SGB application to Long COVID patients and improvement in their symptoms after the procedure [9-11]. Although Luke D. Liu et al. [9] reported complete recovery of olfactory and gustatory dysfunctions at 2-month follow-up in their case series, in our cases we observed 90% recovery in the first patient and roughly 40% recovery in the second patient. The lack of desired improvement of gustatory and olfactory dysfunction in our second case may be because the patient had 2 times SARS-CoV-2 infections 8 months apart, and a larger area of the sensory epithelium was affected, possibly with a more profound destruction of the epithelium that included the death of a larger number of sensory receptor neurons [21]. On the other hand, headaches were completely resolved in both of our cases. The fact that in both previous reports and in our cases, significant improvement in all other symptoms, such as impaired concentration, sleep disturbance, fatigue and myalgia, was seen shortly after SGB may be a basis for the important role of dysautonomia in the pathophysiology of Long COVID cases.

There are also publications on the successful results of SGB application in cases with olfactory sensory impairment due to different etiological conditions [22-24]. A study by Lee et al [25] showed that superior cervical ganglionectomy enhanced the regeneration of olfactory receptor cells in zinc sulfate-induced mouse anosmia. Ho Sik Moon et al. [22] reported that of 37 patients with anosmia or hyposmia with different etiologies, 15 (40.5%) responded to SGB with significant improvement in their symptoms.

Conclusion
The absence of reliable and effective treatment for olfactory, gustatory and other symptoms associated with dysautonomia in Long COVID cases makes SGB an interesting therapeutic option for these patients. However, evidence for the use of SGB to attenuate persistent parosmia and dysgeusia is limited by a few case reports. More evidence needs to be collected by conducting well-designed, multicenter studies to support the use of SGB as a therapeutic modality for the treatment of dysautonomia-associated long COVID symptoms.

Conflict of interest statement: The author declares that he has no conflict of interest.

References


