

## CASE REPORTS

# Sphenopalatine ganglion block for refractory COVID-19 headache: a descriptive case series



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**Abstract** Coronavirus SARS-CoV-2 is responsible for the COVID-19 pandemic, and headache is reported in 6.5% to 34% of all cases. There is little published evidence on the pharmacological treatment of COVID-19 headache. This case series presents six COVID-19 infected patients with refractory headache in which intranasal bedside Sphenopalatine Ganglion Block was performed for analgesia. All patients had a reduction in headache intensity from severe to mild or no pain after the procedure with minor transient side effects. Proposed mechanisms of action include reduction of local autonomic stimuli, intracranial vasoconstriction, and reduction of vasoactive substances release in the pterygopalatine fossa.

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## Introduction

Coronavirus SARS-CoV-2 is responsible for the COVID-19 pandemic. Symptoms vary from asymptomatic patients to severe illness and death. The disease most commonly involves the respiratory tract. However, neurological symptoms are reported in up to 36% of COVID-19 patients, including headaches, impaired consciousness, ataxia, acute cerebrovascular disease, seizures, hyposmia, hypogeusia,

and neuralgia. Headache alone is reported in 6.5% to 34% of all COVID-19 patients. In most infected patients, headache is reported as the sole neurological symptom, with no signs of meningeal irritation.<sup>1,2</sup>

It is postulated that the occurrence of isolated non-specific headache in the absence of other neurological symptoms suggests mechanisms likely to be due to the systemic illness, rather than a primary invasion of the central nervous system by the virus.<sup>1,2</sup> There is little published evidence on the pharmacological treatment of COVID-19 non-specific headache. Anticonvulsants, Calcitonin Gene-Related Peptides (CGRP) monoclonal antibodies, sumatriptan, and non-steroidal anti-inflammatories have

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been proposed as rescue treatments in some cases with limited effect.<sup>2</sup>

Sphenopalatine Ganglion Block (SGB) was first described in 1908 for non-trigeminal facial neuralgia. The sphenopalatine ganglion is an extracranial parasympathetic ganglion located in the pterygopalatine fossa, which lies posterior to the middle nasal turbinate and maxillary sinus, and has multiple autonomic and somatic neural connections to the head, neck and shoulder. Nowadays, SGB is used to treat a variety of conditions, including migraine headache, cluster headache, postdural puncture headache, and second division trigeminal neuralgia, and has a possible role in reducing opioid consumption after sinus surgery.<sup>3,4</sup>

Several techniques have been developed to perform SGB. Recently, the intranasal approach has been used in several studies. It is a simple, bedside technique that can be easily performed with a cotton-tip applicator or catheter and local anesthetic. In this technique, the patient is placed in the supine position with the cervical spine extended. The depth of cotton-tipped applicator advancement is estimated by the measurement of the distance from the opening of the nares to the mandibular notch directly below the zygoma. The cotton-tipped applicator is soaked in local anesthetic and advanced into the nares parallel to the zygoma with the tip angled laterally until it lays on the nasopharyngeal mucosa posterior to the middle nasal turbinate. The applicator may be left in position from 5 to 30 minutes for the local anesthetic to reach the pterygopalatine fossa by diffusion across the nasal mucosa.<sup>3-5</sup>

Given the extensive use of SGB for several primary headaches, it could be a useful technique to treat COVID-19 non-specific headache. This case series presents six COVID-19 patients in which intranasal bedside SGB was performed with a cotton tip applicator and 2% viscous lidocaine to treat refractory headache.

## Case series

Patient 1 is a 28-year-old female with no previous comorbidities. Admitted with COVID-19 respiratory symptoms, holocranial pulsatile headache, and anosmia, with no other neurologic symptoms. The headache was refractory to amitriptyline 25 mg.day<sup>-1</sup>, metimazole 6 g.day<sup>-1</sup>, parecoxib 80 mg.day<sup>-1</sup> and sumatriptan 25 mg tablets. After SGB, there was immediate headache resolution with no recurrence in the next two days.

Patient 2 is a 45-year-old female, with a history of hypertrophic cardiomyopathy and depression, previously using atenolol 75 mg.day<sup>-1</sup> and desvenlafaxine 50 mg.day<sup>-1</sup>. Admitted a few weeks after the resolution of COVID-19 respiratory symptoms with a sole complaint of holocranial pulsatile headache, normal CT scan, and no other neurological symptoms. The headache was refractory to desvenlafaxine 50 mg.day<sup>-1</sup>, acetaminophen 3 g.day<sup>-1</sup>, ketoprofen 200 mg.day<sup>-1</sup>, and sumatriptan 50 mg tablets. SGB was performed with a significant reduction in the pain score from severe to mild pain, which was resolved in the next two days with the same analgesic regimen, and did not relapse.

Patient 3 is a 46-year-old female with no previous comorbidities. Admitted with COVID-19, presenting mild respiratory symptoms, asthenia, nausea, vomiting, anosmia,

and a holocranial pulsatile headache, with no other neurological symptoms. The pain was refractory to metimazole 4 g.day<sup>-1</sup>, codeine 40 mg.day<sup>-1</sup>, amitriptyline 25 mg.day<sup>-1</sup>, and acetaminophen 2.25 g.day<sup>-1</sup>. SGB was performed with a significant reduction in the pain score from severe to mild pain, which was resolved in the next two days with the same analgesic regimen and did not relapse.

Patient 4 is a 36-year-old female with no previous comorbidities. Admitted with dyspnea, nausea, coughing, dorsal pain, and holocranial pulsatile headache with no other neurological symptoms. Pain was refractory to amitriptyline 25 mg.day<sup>-1</sup>, baclofen 10 mg.day<sup>-1</sup>, tramadol 400 mg.day<sup>-1</sup>, and metimazole 8 g.day<sup>-1</sup>. After SGB, the patient reported a 50% improvement in pain symptoms. SGB was performed again with the same technique, after which the patient reported complete headache resolution, with no recurrence in the next two days.

Patient 5 is a 36-year-old female, with a previous history of migraine, treated with prophylactic amitriptyline 25 mg.day<sup>-1</sup>. After a COVID-19 diagnosis, the patient was admitted with mild respiratory symptoms, anosmia, and headache. The headache was described as pulsatile and similar to the previous migraine episodes; however, the usual episodes were unilateral, and the current episode was holocranial. Headache was refractory to amitriptyline 25 mg.day<sup>-1</sup>, dexamethasone 8 mg.day<sup>-1</sup>, metimazole 8 g.day<sup>-1</sup> and pregabalin 75 mg.day<sup>-1</sup>. After SGB, the patient reported complete headache resolution, with no recurrence until discharge.

Patient 6 was a 41-year-old female, with a previous history of obesity and deep venous thrombosis in the right popliteal vein. Admitted with COVID-19 and experiencing dyspnea and headache. Respiratory symptoms resolved rapidly while the headache was refractory to amitriptyline 25 mg.day<sup>-1</sup>, pregabalin 225 mg.day<sup>-1</sup>, metimazole 8 g.day<sup>-1</sup>, acetaminophen 2.25 g.day<sup>-1</sup>, and parecoxib 80 mg.day<sup>-1</sup>. In the clinical examination, the patient had signs of occipital neuralgia as well as non-specific holocranial pulsatile headache. SGB and bilateral occipital greater and lesser occipital nerve block were performed successfully. There was an immediate resolution of the headache with no recurrence in the next three days (Table 1).

## Discussion

This study presents a case series of six patients with refractory COVID-19-related headaches successfully treated with intranasal bedside SGB. In one patient, SGB was repeated after a 50% reduction in pain, followed by 100% pain reduction after the second block. In another patient, bilateral greater and lesser occipital nerve blocks were performed due to an associated occipital neuralgia. All patients had a reduction in headache intensity from severe pain to mild or no pain after the procedure, with no recurrence in the following days until discharge. Only one patient had a previous history of chronic headache, however this patient reported holocranial symptoms instead of the usual unilateral headache. No patients had other neurological symptoms that could point to a differential diagnosis or viral encephalitis. The only other neurological symptom experienced in this case series was anosmia in some patients.

**Table 1** Summary of clinical information.

	Initial headache severity	Headache pattern	Response to Triptans	Number of blockades necessary for pain control	Headache severity after blockades	Pain recurrence after blockades
Patient 1	Severe	Holocranial pulsatile	No response	1 (SGB)	No pain	No
Patient 2	Severe	Holocranial pulsatile	No response	1 (SGB)	Mild pain	No
Patient 3	Severe	Holocranial pulsatile	-	1 (SGB)	Mild pain	No
Patient 4	Severe	Holocranial pulsatile	-	2 (SGB)	No pain	No
Patient 5	Severe	Holocranial pulsatile	-	1 (SGB)	No pain	No
Patient 6	Severe	Occipital + Holocranial pulsatile	-	1 (SGB) + bilateral occipital greater and lesser occipital nerve block	No pain	No

There was significant variability in the initial headache treatments between the six presented cases. This variation could be explained by the fact that different patients were treated by non-specialist physicians from different medical teams before pain staff consultation, resulting in different prescriptions. There is also limited evidence as to which treatment could be effective for COVID-19 headache, with few published case reports on the subject and a lack of consensus.<sup>2</sup> Patients from this case series experienced pain despite a variety of treatments combining sumatriptan, metimazole, acetaminophen, amitriptyline, anticonvulsants, opioids, and baclofen. SGB was indicated only to patients experiencing a headache refractory to treatment, considered by the neurology staff as a lack of response to at least three analgesics with different mechanisms of action.

Minor complications of the intranasal SGB include epistaxis, lacrimation of the ipsilateral eye, anosmia, transient anesthesia, or hypoesthesia of the nose root, pharynx, and palate. Major complications include infection or hematoma.<sup>3–5</sup> In this case series, no patient had epistaxis, hematoma, lacrimation, or signs of infection; however, anosmia and hypoesthesia of the nose root, pharynx, and palate were present in all six cases. These effects were transient and reversed in a few hours. Patients who had hyposmia or anosmia as COVID-19 symptoms did not recover from these symptoms after SGB.

This study suggests that SGB can be an effective analgesic technique to treat refractory headache in COVID-19 patients. There is evidence that this procedure reduces autonomic stimuli to the head, neck, and shoulder, which can explain its effects on pain with an autonomic-mediated component. Other evidence suggests that SGB promotes mild intracranial vasoconstriction, which has an analgesic effect in vascular headaches. There is also limited evidence that SGB could reduce the local release of vasoactive sub-

stances in the pterygopalatine fossa, including calcitonin gene-related peptide (CGRP), indicating a mechanism of action similar to CGRP monoclonal antibodies, which have been used to treat migraines.<sup>4,5</sup> However there is still limited evidence on the reduction of vasoactive substances in response to SGB and more evidence is necessary to support this mechanism of action.

This study has several limitations, including the observational retrospective design, non-standardized of analgesic protocols, and small sample size. However, it is the first report of SGB efficacy for treating COVID-19-related headache. Additional studies, especially with a more robust design, could further contribute to the evidence on this theme.

## Conflicts of interest

The authors declare no conflicts of interest.

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