Treatment of persistent postoperative hiccups with stellate ganglion block
Three case reports

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Abstract
Rationale: Although persistent postoperative hiccups can cause various problems (such as sleep disorders, depression, fatigue) for the patient, there has been little research on this topic. The purpose of this study is to determine the effectiveness of treating persistent postoperative hiccups with a stellate ganglion block (SGB), an injection of local anesthetic in the sympathetic nerve tissue of the neck.

Patient concerns and diagnoses: Three patients each developed persistent hiccups within 3 days of abdominal surgery, lasting for 3 to 6 days. The patients were diagnosed as having persistent hiccups based on the hiccup duration.

Interventions and outcomes: The 3 patients were treated with an SGB. After the procedure, the frequency and intensity of hiccups decreased and then the hiccups stopped completely.

Conclusion: An SGB is an effective method that can be considered in conjunction with other treatments for persistent hiccups. Clinicians should be mindful of the negative effects that persistent hiccups can exert on patients.

Abbreviations: EKG = electrocardiogram, NE = norepinephrine, NGF = nerve growth factor, PFT = pulmonary function testing, SGB = stellate ganglion block.

Keywords: persistent hiccup, post-operative hiccup, stellate ganglion block

1. Introduction

Hiccups can be defined as an involuntary and persistent contraction of the diaphragm and respiratory muscles, followed by sudden closure of the glottis.[1] Based on the duration, hiccups can be categorized as temporary (<48 h), persistent (48 h–1 month), or intractable (>1 month).[2] Despite the low prevalence in general hospitalized patients (54 per 100,000, 0.054%), hiccups are relatively common symptoms in progressive cancer patients, with reported prevalence of 3.9% to 4.5%.[3,4] Temporary hiccups are not very harmful and remedies such as drinking water or holding the breath can alleviate the symptoms. However, persistent or intractable hiccups can induce sleep disorders, exhaustion, fatigue, depression, malnutrition, weight loss, and dehydration. Furthermore, hiccups may induce opening of abdominal or thoracic open surgical wounds, and these patients require active treatment for hiccup symptoms.[5,6]

Various pharmacological and non-pharmacological interventions have been used to treat hiccups. Nonetheless, there is no clear guideline for treatment of hiccups in these patients. Stellate ganglion block (SGB) has been used for treatment of not only traditional symptoms (i.e., angioneurotic disorders and reflex sympathetic dystrophy) but also various other clinical symptoms of unknown origin (including ophthalmologic, otolaryngologic, and other diseases, as well as facial, upper limb, and chest pain).[7] To our knowledge, this is the first case report (with literature discussion) on multiple patients with persistent postoperative hiccups who were successfully treated with SGB. All patients in this case report agreed with the content and provided written consent for publication.

2. Case presentation

2.1. Case 1

A 70-year-old male (weight 71.7kg, height 174.4cm) began experiencing hiccups 1 day after posterior sectionectomy for liver metastasis from rectal cancer, with persistence for 3 days. Consequently, the patient was transferred to the department of anesthesiology and pain medicine. The frequency of hiccups was 10 to 15 times per minute, and the patient had pain induced by persistent hiccups to the extent that he could not sleep. Drinking warm water only alleviated the symptoms for about 30min. He had undergone a Miles’ operation for rectal cancer a year prior, as had hypertension and diabetes. However, he did not experience hiccups after previous surgery. Results of preoperative physical examinations, laboratory findings, simple chest X-ray, an electrocardiogram (EKG), pulmonary function testing (PFT), and echocardiography were normal, and hypertension and diabetes were well managed with medication. There were no
abnormalities observed during surgery, and the patient was transferred to the ICU for general postoperative care, where vital signs remained normal. On postoperative day 1, the L-tube inserted for surgery was removed and the patient was transferred to the general ward.

At the time of consultation, the patient was experiencing pain at the surgery site and sleep deprivation caused by hiccups, but did not exhibit anxiety about the surgical outcome. He was diagnosed with persistent hiccups that required active medical treatment, and was given oral baclofen 10mg twice daily and left SGB was planned. The surgical risks were explained to the caregiver, who gave consent.

For the SGB procedure, the patient was placed supine with the neck slightly elevated and head slightly rotated to the right. A large skin area was sterilized to prevent infection. To avoid pleural damage, a 25-G butterfly needle was inserted between the trachea and carotid sheath at the height of the anterior tubercle at the left transverse process of the 6th cervical vertebra (C6) and cricoid cartilage. When inserting the needle, we palpated the anterior tubercle of C6, simultaneously pushed the sternocleidomastoid muscle and carotid artery outward, and inserted the needle toward the C6 vertebral body. When the vertebral body was reached, we withdrew the needle 1 to 2mm and ensured that no blood was being aspirated. After injecting 0.5mL of 0.2% ropivacaine for initial testing, we confirmed no abnormalities and injected 8mL in total. Immediately after the procedure, we observed Horner syndrome – an indication that SGB was successfully completed – on the same side that was treated. The patient was placed in supine position for pain management (1h), and we confirmed that there were no complications such as phrenic nerve or recurrent nerve injury. Two hours after the procedure, the hiccups stopped but recurred for about 30 more minutes. However, the frequency and duration gradually decreased, and the patient eventually stopped hiccupping.

Although his symptoms did not recur, we repeated left SGB on the following day for prevention and stopped baclofen. The patient was discharged after 1 week and reported on a follow-up phone call that he had not experienced any hiccups since being discharged. At his outpatient clinic visit 3 months after the procedure, he reported that he had not experienced recurrent hiccups.

2.2. Case 2
A 68-year-old male (weight 69.4kg, height 167.4cm) who underwent distal gastrectomy and gastrojejunostomy for gastric cancer developed hiccups on postoperative day 2, when he was transferred to the department of anesthesiaology and pain medicine. The frequency of hiccups was about 40 per minute, and the patient was experiencing disrupted sleep and sometimes nausea and vomiting when the hiccups became severe. His history of hypertension was managed with oral medication, and he had undergone spinal stenosis surgery 10 years prior. Results of preoperative physical examinations, laboratory findings, simple chest X-ray, EKG, PFT, and echocardiography were normal and no abnormalities were observed during or after surgery. Starting the day that hiccupping began, he was given oral chlorpromazine 25mg once daily for 2 days but the frequency and duration of hiccups did not improve. Despite increasing the dose to 50mg, his symptoms did not improve after 4 days. At the time of consultation, he reported slightly reduced frequency and duration of hiccups compared to the day before. Nonetheless, he was still experiencing disrupted sleep, nausea, and vomiting. He was diagnosed with persistent hiccups, and underwent left SGB with 0.2% ropivacaine 8mL using the same method as described above. After the procedure, we observed Horner syndrome, suggesting successful procedure completion. Although his symptoms stopped immediately, the hiccups returned about 2h after the procedure – along with resolution of prosis – with reduced frequency (about 10 times per minute) but increased intensity. For additional treatment, oral baclofen 10mg twice daily was given.

The patient experienced intermittent hiccups until the next morning, and we performed a second SGB on the left side. Similar to the day before, the hiccups stopped immediately after the procedure, but recurred with resolution of prosis. However, the frequency was reduced and the intensity was weakened to an extent where the patient felt much more comfortable. He experienced intermittent hiccups until the next morning, but had no trouble with sleep. Another SGB was performed, but on the right side this time. Hiccups stopped immediately after the procedure, returned 2 to 3h later, and eventually resolved after several hours. We stopped baclofen and the patient was discharged after 3 days without hiccups. At the outpatient clinic visit 4 months later, he reported that he had not experienced recurrent hiccups.

2.3. Case 3
A 44-year-old male (weight 75.4kg, height 170.3cm) who underwent a Whipple procedure with small bowel resection and anastomosis for duodenal cancer began experiencing hiccups immediately after surgery, and was transferred to the department of anesthesiology and pain medicine. The frequency of hiccups was 10 to 20 times per minute, and the intensity worsened if he consumed food or drank water. This patient had no other medical history. Results from preoperative physical examinations, laboratory findings, simple chest X-ray, EKG, PFT, and echocardiography were normal and no abnormalities were observed during or after surgery. After consultation, the patient preferred pharmacological treatment and was given oral baclofen 10mg twice daily. By the next day, hiccups stopped after dosing, but resumed an hour later. We then increased the baclofen to 10mg 3 times daily.

Despite 3 days of baclofen, the frequency and intensity of hiccups remained unchanged. Because of persistent hiccups, the patient underwent left SGB with 0.2% ropivacaine 8mL and we observed Horner syndrome. The frequency and intensity of hiccups were reduced, and the patient stopped hiccupping 2 days after the procedure. We stopped baclofen the day after the procedure, after confirming that hiccups did not recur.

However, on day 10 after the procedure, the hiccups resumed at lower frequency and intensity. We restarted baclofen 10mg 3 times daily and performed a right SGB. After the procedure, the frequency of hiccups worsened but the frequency decreased. Additional left SGB was performed 2 days later, and the hiccups disappeared, although baclofen was continued for 3 additional days. The patient was discharged a week later, and did not experience recurrent hiccups during a year of follow-up.

3. Discussion
Hiccups can develop – even without specific underlying disease – from stimulation of nerve branches above the vagus or diaphragm. Stomach expansion caused by excessive eating, spicy food, liquid consumption, ingestion of air, or stress-related factors (i.e., anxiety) can be contributory. Persistent hiccups
can arise from psychological or idiopathic causes, but are mostly associated with underlying diseases. These include central nervous system lesions or tumors, esophagitis, stomach expansion, ileus, infection, and stimulation of the peripheral nervous system in the head and neck, chest, or abdomen due to surgery or other procedures. In other words, all events that lead to stimulation of the vagus nerve can cause hiccups. Although a definite pathophysiological mechanism of hiccups is yet to be discovered, based on previous studies, it is thought that the hiccup reflex arc plays an important role.

The hiccup reflex arc is composed of afferent, central, and efferent limbs. The afferent limb includes the vagus nerve, phrenic nerve, and the sympathetic chain in the lower chest (T6–T12). The central limb – surrounded by the brainstem, midbrain, reticular formation, and hypothalamus – connects the afferent and efferent limbs. The efferent limb consists of the phrenic nerve (C3–C5), anterior scalene muscle innervation (C5–C7), recurrent laryngeal nerve (branching from the vagus nerve of the glottis), and accessory nerves leading to the intercostal muscles (T1–T11). Under conditions that stimulate the reflex arc, the patient may experience persistent hiccups. Hansen and Rosenberg reported that patients often developed hiccups within 1 to 4 days after abdominal surgery, and that persistent postoperative hiccups could develop if a patient experienced stimulation or expansion of the stomach, a metabolic disorder, electrolyte imbalance, subphrenic abscess, or infection near the reflex arc (i.e., pneumonia). The patients in this case developed hiccups within 4 days of surgery, suggesting that direct damage or morphological changes in the stomach due to surgery may have stimulated the afferent limb of the hiccup reflex arc and caused persistent hiccups. Furthermore, for the patient with worsening symptoms after food or water consumption, expansion of the esophagus or stomach may be the main contributor.

Treatment of persistent hiccups is nonspecific. Nonpharmacological treatments involve stimulation and suppression of the vagus nerve, with tongue lifting, ingestion of highly concentrated sugar water, stimulation of the pharynx, compression over the eyeball or carotid artery, a valsala maneuver, and rebreathing. Pharmacological treatments include anticonvulsants (i.e., phenytoin, carbamazepine, and valproic acid), gamma-aminobutyric acid (GABA), and serotonin (5HT). If these fail, nerve blocking procedures and surgical treatments can be performed. Nonetheless, no treatment method ensures complete cure for the majority of patients.

Although the mechanism of action of SGB in our patients with persistent postoperative hiccups is unclear, some potential mechanisms are suggested. First, SGB may have blocked the sympathetic nerve in the afferent limb of the hiccup reflex arc, which may have effectively alleviated the symptoms. SGB causes blockade of the lower or upper cervical vertebral sympathetic nerves through perineural injection of local anesthetic, with spread of the anesthetic into nearby structures to induce cervicothoracic denervation. Thoracic sympathetic nerve fibers originating from the spinal cord enter into the sympathetic nerve branch leading to the brain through the cervicothoracic ganglion, and SGB may have blocked this pathway. The mechanism is similar to that of thoracic epidural nerve block, which is used to block the afferent limb of the hiccup reflex arc. Second, SGB may have affected the central limb of the hiccup reflex arc to alleviate the symptoms. The mechanism is similar to that of SGB for treatment of facial flushing, complex regional pain syndrome, and posttraumatic stress disorder. The level of nerve growth factor (NGF) in the brain increases in response to acute or chronic stress. The NGF diffuses back toward the cervicothoracic ganglion and promotes growth of sympathetic nerve terminals. Consequently, the level of norepinephrine (NE) in the brain increases, inducing various diseases. SGB acts against this mechanism and reduces the levels of NGF and NE to alleviate the symptoms. This mechanism is associated with the effectiveness of acupuncture treatment for hiccups. When patients with persistent hiccups were treated with acupuncture, the secretion pattern of neurotransmitters and neurohormones (i.e., NE, Gamma-aminobutyric acid (GABA), and serotonin in the brain) was altered. The central limb of the hiccup reflex arc is affected by neurotransmitters in the brain, and control of the neurotransmitters in the brain by SGB may have alleviated persistent hiccups. Third, SGB may have affected the efferent limb of the hiccup reflex arc including the phrenic nerves (C3–C5) and anterior scalene muscle innervation (C5–C7). Ganglia of the sympathetic nerve terminals are interconnected and this complex is connected to spinal nerves through gray rami communicantes. Therefore, blockade of the cervicothoracic sympathetic ganglion may have affected the phrenic nerve and anterior scalene muscle innervation which is connected to the spinal nerves.

In this case report, we performed SGB using a blind method and injected a relatively greater amount of local anesthetic compared to that used in ultrasound-guided injection. Kapral et al. found that ultrasound-guided SGB, as compared with the blind technique, used a lower volume of local anesthetics (5 mL rather than 8 mL). Left SGB was preferred by practitioner. One time right SGB was performed, because patient felt uncomfortable for the left side. The injected drug spread to the vagus nerve and may have caused direct blockade of nearby phrenic nerves, anterior scalene muscle innervation, and recurrent laryngeal nerves, consequently stopping hiccups in these patients. However, the patients did not experience typical symptoms that can occur after phrenic nerve or recurrent laryngeal nerve blockade (i.e., hoarse voice or discomfort during respiration), suggesting that the above scenario is an unlikely explanation.

In conclusion, additional studies should be performed to clarify the mechanism of action for SGB. However, the procedure is a convenient, safe, and effective method that can be considered in parallel with other treatments for persistent hiccups.Clinicians should be aware of the negative effect of persistent hiccups on the quality of life, and should provide adequate and active treatment if necessary.

**Author contributions**

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