Investigation of the swallowing function using interferential current sensory stimulation for Parkinson's disease patients: a single arm intervention study

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Abstract

Aspiration pneumonia is the leading cause of death in patients with Parkinson's disease. The incidence of silent aspiration is high in such patients owing to decreased pharyngeal and laryngeal sensation; thus, interventions for this condition may help prevent pneumonia. In this single-arm, open-label study, we used a cervical percutaneous interferential current stimulation device to activate pharyngeal and laryngeal sensory nerves. We evaluated its effectiveness in patients with Hoehn–Yahr stages 2–4 Parkinson's disease. The primary endpoint was the proportion of patients with a normal cough reflex after consuming 1% citric acid at the end of the intervention compared with baseline measurements. In total, 25 patients received neck percutaneous interferential current stimulation for 20 min twice weekly for 8 weeks. Afterward, the proportion of patients with a normal cough reflex after 1% citric acid consumption increased significantly ($p=0.001$), whereas other indicators such as tongue pressure and peak expiratory flow remained unchanged. A longer duration of illness, higher Unified Parkinson's Disease Rating Scale total scores, and higher levodopa equivalent daily doses were significantly associated with improved cough test outcomes. Hence, cervical percutaneous interferential current stimulation significantly improved cough reflexes and may improve silent aspiration.

1. Aim of Research

Neurological disorders often induce dysphagia, elevating the risk of aspiration pneumonia, affecting patients' prognosis and outcomes, and consequently increasing medical and caregiving costs. Among these neurological disorders, Parkinson's disease (PD), often referred to as "Parkinson's pandemic," is one of the most common diseases with a rapidly rising global incidence. Aspiration pneumonia is a leading cause of death in patients with PD. Therefore, evaluating and developing appropriate and effective interventions for preventing pneumonia are crucial. In particular, patients with PD have a high incidence of silent aspiration owing to decreased pharyngeal and laryngeal sensation, necessitating interventions for prevention of pneumonia. Bedside screening methods, such as the citric acid cough test, are frequently used for evaluating silent aspiration, with impaired cough reflexes increasing the risk of aspiration pneumonia.

Treating the underlying disease is the top priority in treating swallowing disorders associated with PD. The treatment of PD mainly involves pharmacotherapy with anti-parkinsonian drugs. However, a combination of interventions is essential to improve and maintain function. Swallowing rehabilitation mainly focuses on strengthening swallowing-related muscle groups, and training is conducted to strengthen the tongue and suprahyoid muscles. Conversely, effective therapy for decline in sensory function, including silent aspiration, has been performed using techniques such as ice massage. However, evidence-based approaches are limited, and effective methods have not been developed because of the nature

of sensory nerves.

Recently, several instruments have been designed to stimulate and modulate neurological functions. One such innovation involves percutaneous electrical neck stimulation, which can enhance neuromuscular function. Various approaches utilizing pulsed current stimulation have proven effective in inducing muscle contractions, showing promise in treating diverse dysphagia conditions and gaining widespread application in clinical settings. However, a notable drawback of this method is the pain and invasiveness associated with muscle contractions. An alternative approach, employing interferential current sensory stimulation, has been studied, which capitalizes on activating peripheral sensory nerves in the pharynx and larynx to increase sensitivity and protect against aspiration. Some studies suggest that electrical stimulation devices can enhance swallowing without necessitating muscle contractions. Furthermore, compared with pulsed currents, interferential currents can penetrate deeper tissues and offer a more comfortable experience to patients. Therefore, they can stimulate sensory nerves in the deeper layers of the pharynx and larynx without causing discomfort, making interferential current stimulation a promising avenue for alleviating dysphagia. Interferential current stimulation enhances saliva production, reduces pharyngeal latency, increases swallowing frequency in healthy individuals, and augments airway sensitivity. Furthermore, cervical percutaneous interferential current sensory stimulation may enhance airway defense and nutrition in patients with dysphagia.

However, the mechanism by which the device improves swallowing dysfunction in patients with neurological diseases and its specific effects remain unknown. This study aimed to utilize a cervical nerve electrical stimulation device to activate sensory nerves in the pharynx and larynx in patients with PD. The sensory functions of the pharynx and larynx were assessed using a cough test.

2. Method of Research & Progression

The single-arm, open-label study was conducted at Hiroshima University Hospital and adhered to the Standard Protocol Items: Recommendations for Interventional Trials reporting guidelines. We investigated the efficacy and safety of cervical percutaneous interferential current stimulation in patients diagnosed with Hoehn–Yahr stages 2–4 PD based on the Movement Disorder Society criteria. We included patients diagnosed with clinically probable or established PD (Hoehn–Yahr stages 2–4) at registration, based on the Movement Disorder Society criteria and their ability to visit the hospital twice a week and provide written informed consent. The inclusion criteria were as follows: (1) stable levodopa dosage for over 1 month and (2) age between 20 and 85 years. The exclusion criteria were as follows: (1) implantation with pacemakers or implantable defibrillators, (2) undergoing treatments with deep brain stimulation, (3) pregnant or attempting to become pregnant, (4) diagnosed with or having a history of head or neck cancer, (5) active pneumonia, and (6) a history of swallowing rehabilitation.

The enrolled patients underwent cervical percutaneous interferential current stimulation for 20 min twice weekly for 8 weeks utilizing a Gentle Stim® (FoodCare Co., Ltd., Kanagawa, Japan) device. Pads were attached to the front of the neck from the lower border of the mandibular angle to the anterior margin of the sternocleidomastoid muscle. This device has an output of 2050 Hz from one pair of electrodes and 2000 Hz from another pair, causing interference within the deep part of the neck and generating a low-frequency interference current (50 Hz) corresponding to the difference in frequencies in the affected area. Thus, the interferential current (50 Hz) had a lower stimulation threshold than that of pulse stimulation, resulting in minimal patient sensations. A unified protocol was followed for stimulation in all the patients, and a maximum stimulation current below the perceived electrical stimulation threshold (2.0–2.5 mA) was utilized.

Evaluations were performed every 4 weeks from the beginning of the intervention to 16 weeks after intervention initiation, excluding VF, which were conducted every 8 weeks from the beginning of the intervention to 16 weeks after. The primary endpoint was the proportion of patients exhibiting a normal cough reflex,

defined as coughing five times or more in 1 min after a 1% citric acid cough challenge at the end of the intervention (8 weeks from initiation of intervention). The secondary endpoints were: 1) proportion of patients with a normal cough reflex after the 1% citric acid challenge, 8 weeks after the last intervention (16 weeks from the initiation); 2) proportion of patients with a cough reflex after the 1% citric acid challenge within the first 30 s (simplified cough test) after the intervention (8 weeks from initiation of intervention); 3) proportion of patients with a cough reflex after the 1% citric acid challenge within the first 30 s (simplified cough test), 8 weeks after the last intervention (16 weeks from initiation of intervention); 4) proportion of patients with normal swallowing status at the end of the intervention (8 weeks from initiation of intervention) (normal swallowing status was defined as an FOIS score of 7 and an EAT-10 score <3); 5) proportion of patients with normal swallowing status 8 weeks after the last intervention (16 weeks from initiation of intervention); 6) proportion of aspiration and penetration observed via VF examination at the end of the intervention (8 weeks from initiation of intervention); 7) proportion of patients with aspiration and penetration revealed via VF examination 8 weeks after the last intervention (16 weeks from initiation of intervention); and 8) incidence of the onset of pneumonia during the 16-week period after initiation of intervention. Safety was evaluated based on skin symptoms at region of electrode attachment and exacerbation of neurological symptoms owing to electrical stimulation of the head and neck.

A cough test was performed while patients inhaled 1% citric acid–physiological saline mist using a portable mesh nebulizer (NE-U22, Omron, Kyoto, Japan). Citric acid was purchased from Kenei Pharmaceutical Co. Ltd. (Osaka, Japan). Patients were verbally instructed to deeply inhale the nebulized citric acid through their mouths. In the original cough test, five or more coughs occurring within 1 min were considered normal. In the simplified cough test, the first cough reflex occurring within 30 s was considered normal.

3. Results of Research

In this study, 27 participants were initially enrolled; however, two individuals withdrew their consent for personal reasons within 4 weeks of participating in the study. Consequently, interventions and evaluations were conducted on 25 participants without deviation. Adverse events related to the intervention, such as worsened cervical skin or neurological symptoms due to stimulation, did not occur.

Anti-parkinsonian medication demonstrated minimal changes throughout the study period. The normal proportions in the cough and simplified cough tests significantly increased over the 8-week intervention ($p=0.001$ and 0.002, respectively). The χ^2 test revealed significant improvements in the cough and simplified cough tests at 4, 8, 12, and 16 weeks compared with baseline (0 weeks) ($p<0.05$). Most patients had an Functional Oral Intake Scale (FOIS) score of 7, except for one with a score of 6. The patient with a FOIS score of 6 had an Eating Assessment Tool-10 (EAT-10) score >3 (indicative of abnormal swallowing). After the 8-week intervention, a significant increase in the number of individuals classified as normal was observed (EAT-10 score < 3; ($p=0.002$). Moreover, 8 weeks after the intervention (16 weeks from initiation), the proportions of individuals classified as normal in the cough test, simplified cough test, and EAT-10 remained significantly higher than those at baseline ($p=0.007$, 0.002, and 0.007, respectively). In contrast, other swallowing-related indicators, such as tongue pressure and peak expiratory flow remained stable throughout the study. No cases of pneumonia were observed throughout the study period.

Overall, 21 participants had abnormal cough test results at baseline, and 12 showed improvements within the normal range by the end of the 8-week intervention. Therefore, a univariate analysis was conducted using the baseline data to examine factors associated with improvement between the 12 individuals who showed improvement and the nine who did not. Longer illness duration, higher Unified PD Rating Scale total scores, and higher levodopa equivalent daily doses (LEDD) were significantly associated with improved cough test outcomes ($p=0.049$, 0.049, and 0.046, respectively). These three factors exhibited

strong inter-correlations, making multivariate analysis challenging. In contrast, four participants had normal cough test results at baseline, but one individual transitioned to an abnormal state at the end of the 8-week intervention. The frequency of cough reflexes per minute decreased from five to three times. However, the simplified cough test remained normal, and this patient had an LEDD of 300 mg.

4. Future Area to Take Note of, and Going Forward

In conclusion, cervical percutaneous interferential current stimulation significantly improved cough reflexes, suggesting a potential contribution in mitigating silent aspiration. Future research should incorporate randomization, explore stimulatory conditions, and include physiological and biochemical evidence to further investigate this phenomenon.

5. Means of Official Announcement of Research Results

The following has been presented and published as research outcomes.

1) Nakamori M, Toko M, Yamada H, Hayashi Y, Yoshikawa K, Yoshikawa M, Nagasaki T, Hiraoka A, Shimizu Y, Mikami Y, Maruyama H. Impact of neck percutaneous interferential current sensory stimulation on swallowing function in patients with Parkinson's disease: A single-arm, open-label study protocol. Contemp Clin Trials Commun. 2023 Jun 10;33:101158. doi: 10.1016/j.conctc.2023.101158. PMID: 37342176; PMCID: PMC10277457.
2) Nakamori M, Toko M, Yamada H, Hayashi Y, Haruta A, Hiraoka A, Yoshikawa M, Nagasaki T, Ushio K, Yoshikawa K, Shimizu Y, Mikami Y, Maruyama H. Detailed findings of videofluoroscopic examination among patients with Parkinson's disease on the effect of cervical percutaneous interferential current stimulation. Front Neurol. 2023 Nov 7;14:1279161. doi: 10.3389/fneur.2023.1279161. PMID: 38020611; PMCID: PMC10664245.
3) Nakamori M, Shimizu Y, Takahashi T, Toko M, Yamada H, Hayashi Y, Ushio K, Yoshikawa K, Hiraoka A, Yoshikawa M, Nagasaki T, Mikami Y, Maruyama H. Swallowing sound index analysis using electronic stethoscope and artificial intelligence for patients with Parkinson's disease. J Neurol Sci. 2023 Nov 15;454:120831. doi: 10.1016/j.jns.2023.120831. Epub 2023 Oct 10. PMID: 37837871.
4) Nakamori M, Toko M, Yamada H, Hayashi Y, Ushio K, Yoshikawa K, Haruta A, Hiraoka A, Yoshikawa M, Nagasaki T, Mikami Y, Maruyama H. Association between motor symptoms of Parkinson's disease and swallowing disorders. Neurol Sci. 2023 Dec 6. doi: 10.1007/s10072-023-07238-1. Epub ahead of print. PMID: 38055077.