Research Protocol

Clinical study on the effect of bilateral high-frequency transcranial magnetic stimulation combined with swallowing training on patients with dysphagia after tracheal extubation

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1. Research Background

In Intensive Care Units (ICUs), a large number of patients experience Post - extubation Dysphagia (PED) due to tracheal intubation. PED is characterized by clinical manifestations such as no obvious swallowing movements, choking when drinking water, and wet vocalization after swallowing. These manifestations can lead to complications including aspiration pneumonia, electrolyte imbalance, and malnutrition, which in turn result in prolonged hospital stays and increased medical costs. Dysphagia is not only a direct issue affecting the life safety of critically ill patients but also a long - term problem after ICU discharge. Seeking effective treatment methods to alleviate dysphagia in PED patients and prevent various complications during ICU hospitalization is both a key and a challenging point in the entire process of critical care rehabilitation treatment, and it is also the focus of modern rehabilitation treatment.

The pathophysiology of acquired swallowing disorders involves iatrogenic trauma to the laryngeal, pharyngeal, and upper tracheal regions caused by endotracheal tubes, tracheostomy tubes, and transesophageal echocardiography probes. Additionally, factors such as neuromuscular impairment related to critical illness, oropharyngeal and laryngeal sensory dysfunction, discoordination between respiration and swallowing, gastroesophageal reflux, and cognitive deficits contribute to these disorders. Currently, the majority of patients with post-extubation dysphagia (PED) are critically ill. Medical practitioners often prioritize the management of the primary disease while overlooking concomitant swallowing impairments, resulting in insufficient awareness of the risks associated with aspiration. In many domestic medical institutions, systematic screening for PED and swallowing rehabilitation protocols remain underdeveloped, and research on the recovery of swallowing function in PED patients is limited. Therefore, it is imperative to focus on identifying ICU patients at risk of post-extubation dysphagia and to explore effective therapeutic interventions for PED.

In 2007, a randomized controlled trial published by Korean rehabilitation experts in the "Clinical Rehabilitation" journal demonstrated that early swallowing rehabilitation treatment for patients with long-term tracheal intubation could reduce the time of oral transfer, pharyngeal transfer, and pharyngeal swallowing efficiency. In recent years, methods such as speech therapy, pharyngeal electrical stimulation, and swallowing oral care intervention have been proven to improve patients' ability to ingest through the mouth, reduce the prevalence of pneumonia and the rate of re-intubation, and thereby shorten the hospitalization period and reduce the social and economic costs of patients. Although some effective methods have been explored in the PED field, research on PED has mainly focused on identifying the risk factors that affect the recovery of

swallowing function in PED patients, enhancing medical staff's awareness of PED, focusing on high-risk groups of PED, and improving clinical outcomes. It was not until 2020 when Chen Huiming et al. applied swallowing function training to ICU patients with acquired swallowing disorders that intervention studies on swallowing recovery after extubation emerged.

Repetitive Transcranial Magnetic Stimulation (rTMS) is a relatively new neuro-regulation technique. It is a painless, non-invasive electrophysiological therapy that acts on the brain. It can transmit pulses through the skull to the cerebral cortex, subsequently causing axonal depolarization, activating the cortex and subcortical networks, and activating neuronal plasticity and enhancing synaptic transmission capacity. In recent years, bilateral high-frequency repetitive transcranial magnetic stimulation has been based on the theory that swallowing-related muscles are controlled by the motor cortex of both cerebral hemispheres. Applying high-frequency rTMS to the bilateral cerebral hemispheres of patients with dysphagia does not need to consider the control issue, and can simultaneously excite the bilateral genioglossus motor cortex, quickly exerting the compensatory effect of the healthy hemisphere, thereby shortening the recovery time of patients with dysphagia and enhancing the rehabilitation efficacy. There are no relevant literature on the intervention of rTMS on PED in domestic and foreign studies. Currently, it is rare to see clinical reports of bilateral high-frequency repetitive transcranial magnetic stimulation combined with swallowing training in the treatment of acquired dysphagia. Therefore, this study applies bilateral high-frequency rTMS combined with swallowing training to PED patients to explore its application value.

2. Aim of this study

This study aims to investigate the therapeutic efficacy of bilateral high-frequency repetitive transcranial magnetic stimulation (rTMS) combined with swallowing training in the management of post-extubation dysphagia. Through a comparative analysis of swallowing training alone versus the combined intervention, the research evaluates their differential effects on swallowing function recovery and complication reduction in patients with acquired dysphagia. By assessing clinical outcomes, swallowing ability metrics, and incidence of severe complications, the study seeks to elucidate the potential advantages of rTMS in neurorehabilitation for dysphagia, thereby contributing novel insights to clinical research on critically ill rehabilitation patients.

3. Methods and design

3.1 Study setting and desig

(1) Study Design

This study is a single-center randomized single-blind parallel-controlled trial.

(2) Generation of Allocation Sequence

The randomization sequence for subject grouping will be generated by research members uninvolved in trial operations and assessments using the SPSS 22.0 statistical software program.

(3) Allocation Concealment

Allocation concealment will be implemented by using the sealed envelope method. An opaque envelope containing the randomized grouping scheme will be prepared, and envelopes will be sequentially opened according to the enrollment order to determine subject allocation.

(4) Allocation Implementation

The allocation sequence will be generated by personnel not participating in the experiment.

Research staff will recruit subjects, and the personnel responsible for generating the allocation sequence will assign the interventions to the subjects based on the allocation sequence.

(5) Blinding

After the allocation of intervention measures, the research subjects will be in a blinded state. This study will adopt a randomized single-blind parallel control design. Repetitive transcranial magnetic stimulation (rTMS) will apply magnetic stimulation to the target brain area for 20 minutes. At the end of the study or when the subjects request to terminate the trial due to severe adverse reactions, the researchers can lift the blinded state.

(6) Sample Size Calculatio

The primary outcome measure of this study was the Functional Oral Intake Scale score. The a priori sample size calculation was performed using the G*Power software (version 3.1.9.7). Based on the existing swallowing treatment research results for post-tracheal intubation dysphagia, the effect size of the FOIS score was calculated. The significance level (α) was set at 0.05 (two-tailed), and the power of the test (1 - β) was set at 0.80. The calculation indicated that at least 26 patients per group were required to detect the expected effect.

The estimated dropout rate during the study was 15%, so 30 patients were planned for each group, totaling 60 patients, to ensure that there were sufficient samples for statistical analysis in the end.

3.2 Participant recruitment

3.2.1 Inclusion Criteria

(1) Age greater than 18 years;

(2) Tracheal intubation for more than 48 hours;

(3) Clear consciousness at the time of assessment, able to understand and follow the simple instructions of the researchers;

(4) Patients have dysphagia, and the Functional Oral Intake Scale (FOIS) assessment is at levels 1-3;

3.2.2 Exclusion Criteria

(1) Previous history of dysphagia;
(2) Undergoing tracheotomy;
(3) History of epilepsy;
(4) Having metal implants in the brain;
(5) Implanted with a cardiac pacemaker;
(6) Under absolute isolation (such as open or infectious pulmonary tuberculosis.

3.2.3 Study Termination Criteria

Development of adverse events or medical conditions contraindicating continued participation; Voluntary withdrawal by the participant; Protocol non-compliance substantially compromising trial outcome assessments.

3.3 Treatment Protocols

Swallowing training Group: Oral and facial function training, sensory stimulation training, airway protection techniques (including Mendelson training, forceful swallowing method and supraglottic swallowing training), swallowing reflex and coordination training, direct feeding training (including guidance on eating environment, placement of swallowing position, selection of foods of different textures and flavors, the most suitable amount for swallowing,

removal of residual substances in the pharynx, etc.) as well as low-frequency pulsed electrical stimulation and other conventional rehabilitation methods.

Swallowing training + rTMS Group: Participants underwent Swallowing training combined with sham rTMS intervention. Swallowing training involves the following aspects: oral and facial function training, sensory stimulation training, airway protection techniques, coordination training of swallowing reflexes, direct feeding training, and low-frequency pulsed electrical stimulation. Before each swallowing training session, bilateral high-frequency rTMS stimulation of the cerebral hemispheres was administered. An 8-shaped coil was used, with the center point of the coil aligned with the stimulation site, and the bilateral oral and tongue regions were stimulated. The 10-20 system electrode placement method was employed to determine the patient's cranial vertex. Two surface electrodes were placed at the patient's mandibular hyoid muscle, and a magnetic stimulation device was used. An 8-shaped coil with a diameter of 70mm was placed 2-4cm forward and 4-6cm outward from the cranial vertex in this area. The coil was moved to induce the maximum motor evoked potential (MEP) in this area to determine the cortical stimulation hotspots of the bilateral hemispheric mandibular hyoid muscles. The minimum stimulation intensity that elicited at least 3 MEP waves with an amplitude > 50μV during 5 MEPs was considered as RMT. If MEP could not be elicited from the affected hemisphere, the corresponding RMT from the healthy hemisphere was used. During rTMS treatment, the stimulation coil was placed at the MEP hotspot of the affected hemisphere's mandibular hyoid muscle. The coil was in contact with the skull surface, with a magnetic stimulation frequency of 10Hz, a stimulation intensity of 90% of RMT, and each sequence lasted for 5 seconds. After each sequence, there was a 55-second interval. The treatment duration was 10 minutes (500 pulses). Subsequently, the same parameters of magnetic stimulation were applied to the same area of the healthy hemisphere, once a day, with each training session lasting 10 minutes.

3.4 Outcomes

3.4.1 Primary parameter

Functional Oral Intake Scale (FOIS):

The evaluation was conducted using the Functional Oral Intake Scale (FOIS), which is divided into 7 levels. The higher the level, the better the oral intake ability. Level 1: Unable to eat orally; Level 2: Dependent on tube feeding for eating, attempting to eat a minimal amount of food or liquid; Level 3: Dependent on tube feeding for eating, consuming single-textured food or liquid orally; Level 4: Completely eating orally with a single texture of food; Level 5: Completely eating orally with multiple textures of food, but requiring special preparation or compensation; Level 6: Completely eating orally without special preparation, but with specific food restrictions; Level 7: Completely eating orally without any restrictions.

3.4.2 Secondary parameters

(1) Wada Drinking Test(WST)

The swallowing function was evaluated using the WST. The patient was seated, and 30 ml of warm water was consumed. The drinking process was observed, and the rating criteria were as follows: Grade I: Completed drinking in one attempt without choking, score 1 point; Grade II: Completed drinking in two or more attempts without choking, score 2 points; Grade III: Completed drinking in one attempt with choking, score 3 points; Grade IV: Completed drinking in two or more attempts with choking, score 4 points; Grade V: Choking occurred multiple times and drinking was difficult to complete, score 5 points.

(2) Degree of swallowing difficulty(GUSS)

Bedside assessment of swallowing disorders was conducted using the GUSS scale, which consists of two parts: the indirect swallowing test and the direct swallowing test. The indirect swallowing test part includes five indicators: attention, voluntary coughing, swallowing saliva, drooling, and voice. The direct swallowing test part includes screening for the swallowing of thick liquid, liquid, and solid foods, respectively, to assess the situations of delayed swallowing, voluntary coughing, drooling, and voice changes. The

total score is 20 points, with 0 to 9 points indicating severe swallowing disorder; 10 to 14 points indicating moderate swallowing disorder; 15 to 19 points indicating mild swallowing disorder; and 20 points indicating no swallowing disorder.

(3) Pneumonia incidence rate

Extract from the electronic medical records whether the subjects had pneumonia 30 days after extubation.

(4) Hospitalization duration

Records the period of time that the patient was hospitalized.

3.5 Statistical Analysis

Statistical analyses for efficacy evaluation were performed using SPSS 22.0. Data are presented as mean ± standard deviation. Between-group differences were compared using independent samples t-tests. Overall differences across time points between groups were assessed via two-way repeated-measures ANOVA or mixed-effects models. If a significant overall effect was detected, pairwise comparisons were conducted using the Sidak method. A threshold of $P < 0.05$ was applied to determine statistical significance.

4. Research Timeline

September 2025 – May 2026: Participant recruitment, intervention implementation, and data collection.

May 2026 – October 2026: Data analysis.

May 2026 – December 2026: Continued data analysis and manuscript drafting.