Stellate Ganglion Block: A Breakthrough Treatment for Post-Stroke Pharyngeal Dysphagia

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Statement

This trial protocol is confidential and intended for distribution to medical experts, researchers involved in the trial, and other staff members associated with the trial, as well as the medical institutions, ethics committees, and contracted research organizations involved in the trial. Except for providing information to the participants, no content of this trial protocol shall be disclosed or made available to any third party without prior written consent from the sponsor. Furthermore, any partial or complete results of this clinical trial, when published externally in societies, journals, etc., require written consent from the sponsor.

CATALOGUE

Co-organizer

N/A

Abstract

Title	**Stellate Ganglion Block: A Breakthrough Treatment for Post-Stroke Pharyngeal Dysphagia**
Drugs	N/A
Approval number of durgs	N/A
Aims	This study aims to explore the efficacy of stellate ganglion block in post-stroke pharyngeal dysphagic patients who received comprehensive rehabilitation.
Design	This was a randomized controlled study
Indications	post-stroke patients with pharyngeal dysphagia
Total cases	65 post-stroke patients with pharyngeal dysphagia were randomly allocated to the observation group (n=33) or the control group (n=32).
Center	*The First Affiliated Hospital of Zhengzhou University*
Research period	2022.6-2023.6
Case selection	The inclusion criteria were: 1) Age between 30 and 80 years; 2) New-onset stroke, confirmed by head CT or MRI; 3) The course of disease between 1 to 6 months; 4) With pharyngeal dysphagia shown by VFSS; 5) Stable vital signs; 6) Voluntary participation in the study. The exclusion criteria were: 1) Allergy to Lidocaine injection or vitamin B12 injection; 2) Severe cognitive impairment; 3) Coagulation disorders; 4) Severe dysfunction of organs including heart, lungs, kidney, liver, etc.; 6) Complicated with other neurological diseases; 7) With severe oral dysphagia (results of the VFSS oral phase as 2 or 3 points); 8) Dysphagia caused by other diseases or reasons.
Study drug	N/A

Plan	All the participants were provided with the comprehensive rehabilitation (routine rehabilitation and swallowing function training). The routine rehabilitation included intervention for risk factors (blood pressure, blood lipids, blood glucose, smoking and alcohol restriction, exercise, etc.) and pharmacological treatment (aspirin, statins, anticoagulants, etc.). Based on these, the observation group was given SGB once a day, with 10 sessions as a course of treatment and each side of the body for one course.
Visit timing	N/A
Procedures	From June 2022 to June 2023, we conducted a randomized controlled clinical study including 65 post-stroke patients with pharyngeal dysphagia who were transferred or admitted to the department of rehabilitation medicine of 3 hospitals in China. All the participants were provided with the comprehensive rehabilitation (routine rehabilitation and swallowing function training). The routine rehabilitation included intervention for risk factors (blood pressure, blood lipids, blood glucose, smoking and alcohol restriction, exercise, etc.) and pharmacological treatment (aspirin, statins, anticoagulants, etc.).
Assessment	Both groups were provided with comprehensive rehabilitation including routine rehabilitation and swallowing function training. Besides, the observation group additionally underwent the stellate ganglion block (SGB). At admission and after 20-day treatment, Kubota water swallowing test, video fluoroscopic swallowing study (VFSS), and Rosenbek penetration-aspiration scale (PAS) were used to assess swallowing function.
Safety indicator	AEs

1. Background

Stroke refers to a pathological state characterized by the abnormal cerebral blood flow leading to the demise of brain cells[1]. It stands as the foremost cause of disability-adjusted life years (47.3%) and mortality (67.3%) among neurological diseases[2]. In China, the annual incidence of new strokes was estimated at approximately 2 million[3]. Moreover, owing to growth and ageing of population, the incidence of stroke has surged by 59.2%, while the rates of disability and mortality have escalated by 21.7% and 36.4%, respectively[4]. Stroke may manifest in motor dysfunction, sensory impairment, cognitive deficits, dysphagia, and various other symptoms, notably, among which, dysphagia represents a severe complication[5]. It was reported that approximately 60% of conscious acute stroke patients exhibited dysphagia, as evidenced by video fluoroscopic swallowing studies (VFSS)[6]. Stroke-related dysphagia refers to the impediment encountered in the transportation of food from the oral cavity to the stomach due to stroke, resulting in the inability to ingest sustenance safely and acquire adequate hydration as well as nutrition[7]. It should be notified that dysphagia is associated with airway obstruction, aspiration, pneumonia, dehydration, malnutrition, and, in extreme cases, mortality[8]. According to the previous study, the mortality rate among dysphagic patients at 30 days was 22.9%, as compared to 8.3% for non-dysphagic patients[9]. Furthermore, even during the subsequent one-year follow-up period, the mortality rate among dysphagic patients remains notably higher than that of their non-dysphagic counterparts[8].

According to the anatomical structures involved in the process of swallowing, the process of ingestion and swallowing can be categorized into the preparatory phase, oral phase, pharyngeal phase, and esophageal phase[10]. Depending on the specific location of brain stroke injury, patients

may present with varying types of dysphagia[11]. Pharyngeal dysphagia refers to the inability of patients to safely and effectively pass food through the pharynx, including delayed initiation of swallowing, repeated swallowing, coughing, hoarse voice, and aspiration[12]. Global guidelines from the World Gastrointestinal Organization indicate that within three days of a stroke, 42%-67% of the patients will experience oropharyngeal dysphagia, with 22%-42% of them experiencing aspiration[9]. In patients with aspiration, the risk of pneumonia increases, significantly raising their mortality[13]. Furthermore, dysphagia can exacerbate patients' mental health, particularly those unable to consume food via mouth, leading to symptoms such as malnutrition, depression, and social withdrawal[14].

At present, effective measures for treating pharyngeal dysphagia in stroke patients are still lacking. Under most circumstances, swallowing function training is the mainstream therapy provided to facilitate the improvement of dysphagia[15]. Fortunately, in our clinical practice, it was observed that stellate ganglion block (SGB) combined with swallowing function training can notably improve the swallowing function of stroke patients with pharyngeal phase dysphagia. Nonetheless, relevant study remains, still, insufficient.

2.Objective

The current study, therefore, was carried out to explore the clinical effect of SGB combined with comprehensive rehabilitation in post-stroke pharyngeal dysphagic patients, mainly on wallowing function and aspiration.

3.Design

3.Type： This was a multicenter randomized controlled study

3.2 Study patient population

From June 2022 to June 2023, we conducted a randomized controlled clinical study including 65 post-stroke patients with pharyngeal dysphagia who were transferred or admitted to the department of rehabilitation medicine of 3 hospitals in China. The inclusion criteria were: 1) Age between 30 and 80 years; 2) New-onset stroke, confirmed by head CT or MRI; 3) The course of disease between 1 to 6 months; 4) With pharyngeal dysphagia shown by VFSS; 5) Stable vital signs; 6) Voluntary participation in the study. The exclusion criteria were: 1) Allergy to Lidocaine injection or vitamin B12 injection; 2) Severe cognitive impairment; 3) Coagulation disorders; 4) Severe dysfunction of organs including heart, lungs, kidney, liver, etc.; 6) Complicated with other neurological diseases; 7) With severe oral dysphagia (results of the VFSS oral phase as 2 or 3 points); 8) Dysphagia caused by other diseases or reasons. The shedding criteria were: 1) Infection at the site of blockade; 2) Patient’s own request; 3) the patient's condition deteriorated severely; 4) death.

3.3Intervention

All the participants were provided with the comprehensive rehabilitation (routine rehabilitation and swallowing function training). The routine rehabilitation included intervention for risk factors (blood pressure, blood lipids, blood glucose, smoking and alcohol restriction, exercise, etc.) and pharmacological treatment (aspirin, statins, anticoagulants, etc.).

Regrading swallowing function training, both groups were given swallowing function training, including 1) exercises of closure of the vocal folds, pharyngeal, and laryngeal muscles exercises, and respiratory muscle strength training, for 15 min each time and twice per day. 2) isotonic / isometric swallowing exercises, supraglottic swallowing exercises, and the Mendelsohn maneuver, for 20 min each time and twice per day. 3) effortful swallowing exercises, and cough reflex training, for 10 min each time and twice per day.

Based on these, the observation group was given SGB once a day, with 10 sessions as a course of treatment and each side of the body for one course. All the materials included: 1) 1.5ml of 2% Lidocaine hydrochloride injection (1ml: 0.5mg), Vitamin B12 Injection 500ug (1ml: 0.5g), the 5 ml disposable syringe and the sterile disposable dental injection needles. The specific operation procedure was as follows[16]: The operator stood at the patient's block side, and the patient was placed in the supine position, with the head leaning 45 degrees toward the

contralateral side of the block side. After routine disinfection of the skin, a paratracheal approach was adopted, which was, 2.5cm above the sternoclavicular joint and 1.5cm outside the midline of the neck. The operator, with the tips of the index finger and middle finger, pushed the trachea and esophagus to the medial side, and the sternocleidomastoid muscle and common carotid artery to the lateral side. Next, the operator inserted the needle vertically until the needle tip reached the C7 transverse process and then withdrew the needle slightly. If there was no blood or cerebrospinal fluid back drawn, the blocking drug should be slowly injected, and the presence of Horner's syndrome indicated a successful block. After the injection, the patient was required to keep lying down for 30 minutes to ensure there were no abnormal symptoms.

4、Case selection

4.1 **The inclusion and exclusion criteria**

The inclusion criteria were: 1) Age between 30 and 80 years; 2) New-onset stroke, confirmed by head CT or MRI; 3) The course of disease between 1 to 6 months; 4) With pharyngeal dysphagia shown by VFSS; 5) Stable vital signs; 6) Voluntary participation in the study. The exclusion criteria were: 1) Allergy to Lidocaine injection or vitamin B12 injection; 2) Severe cognitive impairment; 3) Coagulation disorders; 4) Severe dysfunction of organs including heart, lungs, kidney, liver, etc.; 6) Complicated with other neurological diseases; 7) With severe oral dysphagia (results of the VFSS oral phase as 2 or 3 points); 8) Dysphagia caused by other diseases or reasons.

4.2 **The dropout criteria**

The shedding criteria were: 1) Infection at the site of blockade; 2) Patient’s own request; 3) the patient's condition deteriorated severely; 4) death.

4.3 Termination criteria

If more than half of the subjects experience mild or higher adverse reactions (such as 3/6, 4/8), the trial should be terminated.

5、Study management

5.1 Ethical Considerations and Informed Consent

5.1.1 Approval by an Independent Ethics Committee

Prior to the commencement of the trial, the researcher/research institution should obtain written approval from the independent ethics committee regarding the trial protocol, informed consent form, subject recruitment procedures, and any other written materials to be provided to the subjects. During the course of the trial, if there are any additions or revisions to the trial protocol, informed consent form, etc., written approval from the independent ethics committee should be obtained again.

5.1.2 Informed Consent

The researcher or their designated representative will be responsible for explaining the background of the study, the pharmacological characteristics of the investigational medication, the trial protocol, as well as the potential benefits and risks of participating in the trial to each subject, the subject's legally authorized representative, or witness. They should obtain written informed consent signed by the subject or their legally authorized representative and the investigator before the subject enters the trial (before screening).

The final text of the informed consent form should include the following: the purpose of the trial, trial procedures, the subject's obligations, the foreseeable benefits and risks and inconveniences of participating in the trial, treatment and appropriate insurance compensation

available to the subject in case of trial-related harm, access to trial data, and confidentiality of subject information.

The informed consent form should obtain written approval from the ethics committee and be written in a language that is understandable to the subject. The subject or their legally authorized representative, the researcher conducting the informed consent process, or their representative should all sign and date the informed consent form. The original copy of the informed consent form should be retained by both the researcher and the subject. If important new information related to the investigational drug in a clinical trial is discovered, the informed consent form must be modified in writing, submitted for approval to the ethics committee, and re-obtained from the subject.

5.2 Protection

Prior to the start of the clinical trial, the trial protocol must be reviewed and approved by the ethics committee of the responsible research institution before implementation. Any modifications to the trial protocol during the course of the clinical trial should also be approved by the ethics committee before they can be executed.

Clinical researchers must inform subjects that participation in the clinical trial is voluntary and that they have the right to withdraw from the trial at any stage without facing discrimination or retaliation. Subjects must be made aware that their participation in the trial and their personal information will be kept confidential. They should also be informed about the nature of the clinical trial, the trial objectives, the potential anticipated benefits, and the possible risks and inconveniences. Subjects should be informed of their rights and obligations as outlined in the Helsinki Declaration, and given sufficient time to consider whether they wish to participate in the trial.

5.3 Management Unit

This study will be conducted at the First Affiliated Hospital of Zhengzhou University and will be overseen by the ethics committee of the hospital and the clinical trial institution.

6. References

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