



Original Article

## Efficacy of neuromuscular electrical stimulation on Wilson's disease patients with dysphagia

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**Abstract.** [Purpose] Dysphagia is a neurological symptom that is observed in more than half of patients with Wilson's disease. It is often associated with aspiration pneumonia, dehydration, and malnutrition, resulting in drastic reduction of the quality of life. Neuromuscular electrical stimulation could be an adjunct therapy for dysphagia treatment. However, there is limited data about the application of NMES for dysphagia in Wilson's disease. Thus, we explored the potential application of NMES for dysphagia treatment in Wilson's disease. [Participants and Methods] Sixty Wilson's disease patients who suffered from dysphagia were randomized into two groups. Swallowing function training was taught to the control group (n=30) while Neuromuscular electrical stimulation therapy was given to treatment group (n=30). Eight weeks post treatment, using the water swallow test and the Standardized Swallowing Assessment, the swallowing function was determined. [Results] None of the patients experienced discomfort before, during or after the intervention. After 8 weeks of therapy, when compared to the control, an increased improvement in swallowing function was noted for the treatment group. [Conclusion] Neuromuscular electrical stimulation treatment can improve swallowing function in Wilson's disease patients afflicted with dysphagia. Therefore, it has the potential to be a form of therapy in clinical practice.

**Key words:** Wilson's disease, Dysphagia, Neuromuscular electrical stimulation

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### INTRODUCTION

The autosomal recessive Wilson's disease (WD), a copper metabolism disorder, results in the aggregation of copper, primarily in the kidneys, brain, cornea and liver. This can lead to various clinical conditions associated with neurological, psychiatric, and hepatic symptoms. Patients normally exhibit neurological symptoms in their mid-teens or twenties and in rare cases at later stages of life<sup>1, 2)</sup>. One such symptom is Dysphagia which is associated with more than half of WD patients<sup>1-3)</sup>. Scintigraphic examination revealed that, the features of WD dysphagia on comparison to healthy individuals of the same age were determined to be: slower pharyngeal transit time, increased percentage of oral and pharyngeal residue, prolonged oral transit time<sup>3)</sup>. da Silva-Júnior et al. claimed that copper accumulation in the brain, mainly in the substantia nigra, could lead to pre- and post-synaptic dopamine deficiency, leading to dysphagia<sup>3)</sup>. Due to this there are similar patterns observed in dysphagia in WD and also in Parkinson's disease<sup>3, 4)</sup>. It is often associated with dehydration, malnutrition, and aspiration pneumonia, resulting in reduction of life quality. It hinders the patient's recovery, prolongs the length of hospitalization, increases financial burden, and eventually results in death<sup>1, 5, 6)</sup>. Therefore, effective treatment for dysphagia is required.

While general criteria have been established for dysphagia management, there are very few reports indicating pharmacological and non-pharmacological therapies for dysphagia in WD<sup>1, 4)</sup>. Therefore, there are no specific recommendations for dysphagia treatment in cases of WD<sup>1, 4)</sup>. Neuromuscular electrical stimulation (NMES) was recommended as an adjunct form

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of therapy for dysphagia. It is widely used in clinical practice to improve the swallowing function of patients with various neurological diseases<sup>7-11</sup>). NMES has the ability to stimulate the muscle fibers by stimulating the nerve and the motor end plate of the nerve. This leads to an increase in swallowing muscle strength and sensory awareness, thereby improving or recovering the swallowing function<sup>8, 9</sup>). Lee et al. reported that the dysphagia in one WD patient was improved by NMES, according to improved hyoid bone movement and decreased pharyngeal residue<sup>4</sup>). However, no other reports have been made about the application of NMES for dysphagia in WD. Thus, the detailed regarding the effects of NMES on dysphagia in WD remain controversial because of only one study in which its treatment effect was studied only in one patient, but it was a short term observation and the study lacked controls.

Therefore in this study, we investigated the effectiveness and safety of the NMES in dysphagic patients with WD. It was hypothesized that NMES would contribute not only to a significant improvement of the swallowing function, but would also act without undesirable side-effects in these patients.

## PARTICIPANTS AND METHODS

Sixty WD patients suffering from dysphagia were chosen from the Neurological Department, the first affiliated hospital of Anhui University of Traditional Chinese Medicine, between 2015 and 2018. The diagnosis of WD was based on positive family history, signature clinical manifestations, increased copper levels in the liver (>250 µg/g dry weight), appearance of a K-F (Kayser-Fleischer) ring, increased levels of urinary copper excretion for 24-h after intake of two 500-mg doses of D-penicillamine (>1,600 µg/24 h), elevated levels of copper in urine in 24 h (>100 µg/24 h), and magnetic resonance imaging (MRI) of brain, low serum ceruloplasmin (<0.2 g/L), and were within the WD diagnostic criteria determined at the “8th International Meeting on Wilson disease”<sup>11, 12</sup>). Patients with recent diagnosis were chosen, who had a history of chelation treatment without neurological deterioration. Patients with refractory ascites, severe jaundice; those who were pregnant or lactating; and those with reduced cognition were excluded from this study. None of the patients were using psychotropic drugs. Prior to the procedure, informed consent was acquired. From adult patients, written consent was taken. For children, consent was obtained from their parents or guardians. Approval for this study was obtained from the Institutional Review Board of the First Affiliated Hospital of Anhui University of Traditional Chinese Medicine (Approval number: 2015HGSS01).

Patients were retrospectively divided into 2 groups according to the treatment they underwent. Both groups received the same swallowing function training, which is a basic treatment. The patients treated with a basic treatment, were enrolled in control group. In addition to this basic training, patients in the treatment group were additionally treated with NMES.

Thirty patients (17 males) who had a mean age of  $23.8 \pm 6.28$  years were placed in the control group. The treatment group included 30 patients (16 males) who had a mean age of  $23.6 \pm 6.29$  years (Table 1).

The basic treatment which included pharynx, tongue, and larynx exercises, were taught to patients in accordance with previously reported routine rehabilitation training<sup>9</sup>). Each exercise was practiced for 15 circles at each time resulting in 45 circles a day, 5 days per week for 8 weeks, overseen by a swallowing therapist.

Treatment group patients had additional NMES treatment. Patients were made to recline in a chair and skin electrodes were attached. Using a dual-channel electrotherapy system of VitalStim (Chattanooga Group, Hixson, TN, USA), electrical stimulation was applied. The thyroid notch was determined by palpation and the first electrode was placed midline. 1 mm above and below, the second and third electrodes were placed respectively. The last electrode was placed below the third. NMES was carried out (80 Hz frequency, 0 to 25mA wave amplitude, 700 ms wave width)<sup>9</sup>). The stimulus intensity was slowly amplified (0.5mA at a time), until patients experienced a “grabbing” sensation. Patients were allowed to experience this feeling prior to treatment to prevent false positives. Based on patient feedback, the stimulus was adjusted. On experiencing the grabbing sensation, the electric current was maintained for the rest of the therapy session (1 h)<sup>4, 7-9, 13</sup>). All the evaluations and exercises for both the groups were overseen by the same therapist. The swallowing function was evaluated prior and post 8-weeks of treatment.

To assess the swallowing function prior and post treatment, water swallow test (WST) was carried out<sup>9, 14</sup>). Patients were requested to drink 30 mL lukewarm water. Scores given were tabulated in Table 1. Then, the following grading system was used to describe the swallowing ability: Grade 1, swallowing all water without gagging; Grade 2, swallowing all water in 2 or more attempts without cough; Grade 3, swallowing all water once but with gagging; Grade 4, swallowing all water in two or more mouthfuls with gagging; Grade 5, inability to swallow all water and with constant gagging. A Standardized

**Table 1.** Participants’ characteristics at baseline

Variables	Control group (n=30)	Treatment group (n=30)
Gender		
Male	17	16
Female	13	14
Age (years)	$23.8 \pm 6.28$	$23.6 \pm 6.29$

Values represent Means  $\pm$  SD.

Swallowing Assessment (SSA) identified dysphagia was also rated using the Video Fluoroscopic Swallowing Study (VFSS) as previous studies<sup>11, 15</sup>. SSA includes three parts: 1) clinical examination, including head and trunk control consciousness, spontaneous cough, breathing, lip closure, swallowing reflex, laryngeal function, and soft palate movement, with a total score of 8–23; 2) patients are requested to swallow 5 mL of water thrice and are observed for laryngeal movement, repeated swallowing, wheezing during swallowing and laryngeal function after swallowing, with a total score of 5–11; 3) In the absence of abnormality, patients are requested to swallow 60 mL Water, and are observed for the time needed to swallow, cough and so on, with the total score of 5 to 12 points. The lowest score of the scale is 18, and the highest score is 46. High scores indicate reduced swallowing function.

WST and SSA evaluation were carried out three times by specially trained rehabilitation therapists and after 8-weeks of treatment.

Statistical analysis was carried out with SPSS20.0 (Chicago, IL, USA). Data were expressed as mean ± standard deviation with  $p < 0.05$  as statistically significant. Mann-Whitney U test was used for the result comparison of WST and SSA.

## RESULTS

Based on age, gender, and WST and SSA results between the 2 groups observed on admission, there was no statistically significant difference.

All of the patients completed treatment. None of the patients experienced discomfort before, during or after the intervention. Electrical stimulation could be safely administered with the absence of adverse effects like laryngeal spasm, hypotension, arrhythmia and syncope. After 8 weeks of therapy, it was found that patients showed an improvement in swallowing function which was estimated by WST and SSA. Better improvement was observed in participants of the treatment group ( $p < 0.05$ ) (Tables 2 and 3).

## DISCUSSION

NMES is a noninvasive intervention technology for the management of swallowing disorders. Recently, it has been widely applied in the clinical setting and has shown to be effective in treating dysphagia in various neurological diseases<sup>8–10, 13</sup>. Meng et al. reported that NMES can significantly improve swallowing function in the patients with post-stroke dysphagia<sup>14</sup>. Park et al. considered that NMES is effective in improving the oropharyngeal swallowing function in patients with Parkinson's disease and dysphagia<sup>8</sup>. Toyama et al. suggested that NMES combined with conventional treatment is more effective than conventional treatment alone, in patients with dysphagia following treatment of brain injuries<sup>10</sup>. Similarly, in this study of NMES treatment in WD patients with dysphagia, we also observed an improvement in swallowing function with an absence of adverse effects.

Deglutition is a complex process and its dysregulation may be caused by lesions in any of the structures implicated in the swallowing act, including cortical areas and their efferent pathways, brain stem motor or sensory nuclei, lower cranial nerves, neuromuscular junction and striated muscles<sup>3, 16–18</sup>. The efficacy of NMES could be due to the following reasons<sup>11</sup>: (1) the sensory approach may increase the local sensory input to the central nervous system via the central pattern generator (CPG) which is located in the lower brainstem. This could induce the action of swallowing, therefore eliciting both sensory and motor effects. The sensory stimulation may also have a long-term effect in reorganization of the human cerebral cortex, resulting in the enhancement of brain plasticity/recovery in swallow control. (2) NMES stimulates muscle contraction mainly

**Table 2.** Comparison of the scores of WST prior and post NMES from the two groups

	prior NMES (n=30)	post NMES (n=30)
Control group	4.13 ± 0.58	3.83 ± 0.66
Treatment group	4.05 ± 0.62	3.19 ± 0.69*

Values represent Mean ± SD. \*Significant difference:  $p < 0.05$ .

WST: water swallow test; NMES: Neuromuscular electrical stimulation.

**Table 3.** Comparison of the scores of SSA prior and post NMES from the two groups

	prior NMES (n=30)	post NMES (n=30)
Control group	35.69 ± 3.35	34.96 ± 3.41
Treatment group	35.86 ± 3.29	30.07 ± 2.59*

Values represent Mean ± SD. \*Significant difference:  $p < 0.05$ .

SSA: Standardized Swallowing Assessment; NMES: Neuromuscular electrical stimulation.

via low frequency pulse current. Food is moved into the esophagus by contraction and expansion of the pharyngeal muscle. This helps reconstruct the control function of the brainstem reflex center over swallowing reflex, enhance pharyngeal muscle coordination and flexibility, promote blood circulation, and avoid pharyngeal muscle atrophy. At the same time, with the help of correct pharyngeal stimulation, swallowing function can be improved or restored by increasing the pressure in the mouth. With the help of NMES, the digestive capability of oropharyngeal cavity and esophagus is strengthened<sup>7-9</sup>). Several studies reported the effects of NMES on patients in Parkinson's disease with dysphagia<sup>7, 8</sup>). As a result, improved swallowing function, and reduced aspiration were observed. However, available data on utilization of NMES for dysphagia in WD is very limited. In the current study, it was noted that swallowing function showed only a gradual improvement with the rehabilitation training. On the other hand, a bigger improvement was observed in patients of treatment group. Our study indicated with the help of NMES, that swallowing function of WD patients can be enhanced. Limitation of the study include a small number of participants, lack of long-term follow up and lack of prospective selection of participants. Thus, it is suggested that future studies involve a larger number of participants, and investigation of the long-term curative effects.

In summary, NMES treatment can safely enhance the swallowing function of WD patients with dysphagia. Therefore it has potential application in clinical practice.

### *Conflict of interest*

Authors reported no conflict of interest.

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