Effectiveness of the sequential 4-channel NMES compared with conventional 2-channel NMES for the treatment of dysphagia in a prospective double-blind randomized controlled study

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Running heads: Sequential 4-channel NMES for Dysphagia

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Word count: Abstract: 224, Manuscript: 3439

Numbers of tables and figures : 6

Abstract

Background: To date, conventional swallowing therapies and 2-channel NMES are standard treatments for dysphagia. The precise mechanism of 2-channel neuromuscular electrical stimulation (NMES) treatment has yet to be determined, and controversy remains over the efficacy. The sequential 4-channel NMES was newly developed based on the normal contractile sequence of swallowing-related muscles.

Objective: To evaluate and compare the rehabilitative effectiveness of sequential 4-channel NMES with that of conventional 2-channel NMES.

Methods: In this prospective randomized case-control study, 23 subjects with dysphagia were enrolled. Twelve subjects with 4-channel NMES group and eleven subjects with 2-channel NMES group completed the intervention. Pretreatment and posttreatment evaluations were performed with the videofluoroscopic dysphagia scale (VDS), penetration-aspiration scale (PAS), MD Anderson dysphagia inventory (MDADI), functional oral intake scale (FOIS), and Likert scale.

Results: The sequential 4-channel NMES group significantly improved the VDS (oral, pharyngeal, and total), PAS, FOIS, and MDADI (emotional, functional, and physical scale) compared with pretreatment data. The 2-channel NMES group significantly improved the VDS (oral, pharyngeal, and total) and MDADI (emotional, physical scale), but not the PAS and FOIS compared with pretreatment data. When the two groups were directly compared, the 4-channel NMES group showed significant improvement in oral and total VDS.

Conclusions: Sequential 4-channel NMES activating the suprahyoid, thyrohyoid, and other infrahyoid muscles with proper interval time can be a new effective treatment for dysphagia.

Trial registration number: NCT03670498(clinicaltrials.gov)

Keywords: Deglutition; Dysphagia; Electrical stimulation

Introduction

Dysphagia is a common and serious problem in patients with stroke and the prevalence ranges from 37 to 78%.[1] Decreased laryngeal elevation caused by pharyngeal muscles' weakness is a main cause of dysphagia in these patients, which can result in aspiration and pharyngeal residue during swallowing.[2, 3] Till now, diverse methods, such as oropharyngeal exercises, compensatory maneuvers, neuromuscular electrical stimulation (NMES), and diet control, are used for dysphagia treatment.

To date, most of the clinical studies regarding NMES evaluated the rehabilitative effects after distinct treatment sessions, and 2-channel NMES has been gaining attention for its muscle strengthening effect by motor stimulation and facilitation of swallowing reflex by sensory stimulation.[4] Freed et al. and Blumenfeld et al. indicated that transcutaneous electrical stimulation is superior to conventional dysphagia management probably due to stimulation of the sensory cortex of the cerebrum, recruitment of more motor units rather than volitional contractions, and an increase in local blood flow.[5, 6] However, the precise mechanism of 2-channel NMES treatment has yet to be determined, and controversy remains over the efficacy and method of stimulation.[7] No previous studies have provided the reason for the effectiveness of co-stimulation of suprahyoid and infrahyoid muscles, and a recent randomized controlled trial failed to prove the efficacy of 2-channel NMES in patients with stroke.[8, 9] Moreover, conventional 2-channel NMES does not stimulate the muscles as a physiological sequence of muscle activation during swallowing.[7, 10]

In our previous study, activations of the suprahyoid muscles develop about 150–300 ms earlier than those of the infrahyoid muscles.[10] These sequential contractions of the suprahyoid and infrahyoid muscles induce a circular motion of the hyoid bone during the normal swallowing process, which moves forward-upwardly in the beginning and then backward-downwardly.[11] This result may suggest that simultaneous stimulations of the suprahyoid and infrahyoid muscles could result in the

78 cancellation of positive effects.[12-14] But the previous 2-channel NMES stimulated swallowing
79 related muscles simultaneously, which is different from a physiologic motion. Stimulation of these
80 muscles via the 4-channel NMES may lead to better modifications of the abnormal hyoid and
81 laryngeal motion in patients with dysphagia.

82 Therefore, we hypothesize that the sequential 4-channel NMES based on normal physiology would
83 improve the hyoid and laryngeal motions during swallowing, as well as the swallowing function in
84 general. The purpose of this study was to compare and prove the superiority of sequential 4-channel
85 NMES to 2-channel NMES at pretreatment and posttreatment in a randomized double-blind clinical
86 trial.

87

88 **Methods**

89 ***Study design***

90 This study was a multicenter, prospective, double-blind, randomized controlled clinical trial from
91 July 18, 2018 to August 4, 2019. It was performed at the rehabilitation unit of five teaching hospitals
92 (Seoul National University Bundang Hospital, Seoul National University Hospital, Hallym University
93 Dongtan Sacred Heart Hospital, Daegu-Patima general Hospital, and the Jeju University Hospital).
94 The study protocol was approved by the institutional review board of each hospital (IRB No.: E-
95 1806/475-002, 2018-07-012, JEJUNUH 2018-07-010, J-1810-064-979, DFH19DPOS033) and all
96 methods were performed in accordance with the relevant guidelines and regulations. It was also
97 approved by the Ministry of Food and Drug Safety in Republic of Korea and registered at
98 clinicaltrial.gov (Registration number: NCT03670498, Initial release: 09/13/2018, Actual study start
99 date: 10/01/2018, Actual study completion date: 08/04/2019, Last release: 07/23/2020). All patients or
100 their representatives provided written informed consent prior to participation. A steering committee
101 (Seoul National University Bundang Hospital) was responsible for the design, conduct, and reporting

of the study. Data and safety were monitored every 6 months. The datasets generated and/or analyzed during the study are available from the corresponding author upon reasonable request.

Participants

As the 4-channel NMES was first developed, there was no study before to find out the rehabilitative effect of this equipment. Therefore, we randomly calculated 13 subjects in each group, considering 10% of the dropouts.[15] Participants were recruited from the rehabilitation unit of five teaching hospitals.

Patients were eligible for study participation if they were older than 19 years, presented with cerebral infarction or hemorrhage within 3 months, had at least one symptom of dysphagia such as food sticking, cough with eating, and globus sensation, had confirmed dysphagia by videofluoroscopic swallowing study (VFSS), had stable vital signs, agreed to participate in the present study, and gave informed consent. VFSS criteria included definite presence of aspiration (presence of definite aspiration (penetration-aspiration scale (PAS) $\geq$ 6) or presence of penetration (PAS scale, $\geq$2 and $\leq$5) with residual material at vallecular pouch or pyriformis sinus) to prevent ceiling effect.[16]

The following patients were excluded: those who had severe cognitive dysfunction who could not perform 1 step follow command, serious psychiatric disorder, previous cervical surgery, respiratory difficulty, and cervical surgery. Patients who were pregnant and breast-feeding and those who had cancer and allergic reaction to electrodes of NMES were excluded.

Randomization and masking

Patients were randomly assigned to receive 4-channel NMES or 2-channel NMES (1:1) via computerized random allocation sequences that were prepared by a statistician not involved in

participant recruitment. The randomization schedule was only accessible by 2 individuals: the statistician and the primary investigator (JS Ryu). Group allocation was only accessible to occupational therapists and primary investigator. All participants were blinded to the allocation and four designated areas of the electrodes to guarantee masking. The study group received sequential 4-channel NMES, and the control group received conventional 2-channel NMES. In addition, the investigators involved in outcome assessment (JY Jang, SY Lee, D Park, KH SEO) were blinded to group allocation. This study conforms to all CONSORT guidelines and reports the required information accordingly (see Supplementary Checklist).

Equipment: Sequential 4-channel NMES and 2-channel NMES

The sequential 4-channel NMES was newly developed based on the normal contractile sequence of swallowing-related muscles (Supplementary Figure 1(A); STF-1000, Stratec Co, Ltd, Anyang, South Korea).[10] This device has four channels that are adjustable for amplitude of current, latency, and duration of electrical stimulation. The device uses four pairs of electrodes for electrical stimulation. The electrodes are round in shape and 22 mm in size, and the gap between electrodes consists of two forms: 0.5 cm (type 1 electrode) and 1 cm (type 2 electrode). Type 1 electrode was used for channels 1, 2 and 4, and type 2 electrode was used for channel 3 (Supplementary Figure 1(B); One Bio Medic Co., Ltd, Bucheon-si, Gyeonggi-do, South Korea).

The location of the electrodes was determined using both anatomical landmarks (attachment of each muscle) and manual palpitation. Channel 1 (right) and channel 2 (left) electrodes were placed superior to the hyoid bone and posterior to the mandible with 1-cm interval from the midline, which were targeted for bilateral digastric and mylohyoid muscles. Channel 3 electrodes were placed on bilateral superior pole of the thyroid cartilage for bilateral thyrohyoid muscles, and channel 4 electrodes were placed medial to the sternocleidomastoid muscle and inferior to the thyroid cartilage, which were

148 targeted for the other infrahyoid muscles (sternohyoid, omohyoid, and sternothyroid muscles) (Figure
149 1(A)). In a previous study, a 2-channel NMES on submental and throat stimulations showed better
150 outcome than submental stimulation. The real electrical stimulation was applied to two sets of
151 electrodes attached to the suprahyoid and thyrohyoid muscles (Figure 1(B)).[9] Other electrodes used
152 for sham were only attached, but electrical stimulation was not applied.

153 Electrical stimulation algorithm is based on a previous study.[10, 17] Channels 1 and 2 start
154 electrical stimulation first, and channels 3 and 4 start their stimulations 150 ms and 250 ms later,
155 respectively. The stimulation of channels 1 and 2 lasts 1200 ms, and the stimulations of channels 3
156 and 4 last 1050 ms and 950 ms, respectively. Therefore, channel 1–4 stimulation ends simultaneously
157 in one sequence.[10] Two-channel NMES (Vitalstim®; Chattanooga Group, Hixson, TN, USA) and 4-
158 channel NMES had the same stimulation parameters. The electrical stimulus of NMES device had a
159 continuous symmetric biphasic waveform. The pulse frequency was 80 Hz, and the pulse interval was
160 700 μs. The amplitude for each channel could be independently adjusted between 0 and 25 mA.[18]

161

162 ***Interventions***

163 All participants received 2- or 4-channel NMES for 2–3 weeks (minimal session: 7 times, treatment
164 duration: 420 min–840 min). Treatment durations and daily sessions were different among the 5
165 rehabilitation units and general patients' condition. For example, some patients received once or twice
166 daily 30 min, once or twice daily 40 min, or once daily 60 min treatment. Some patients had difficulty
167 in once daily or twice daily treatment for fatigue or general medical condition. When the participants
168 received once daily 40 min treatment for 2 weeks (10 times) and once daily 60 min treatment for 2
169 weeks, the treatment durations were 400 and 800 min, respectively. We considered a treatment margin
170 of 20 min. Therefore, we set 420 min and 840 min as the minimal and maximal treatment durations,
171 respectively.

Each participant was familiarized with the expected sensations upon use of the surface electrical stimulation unit. Before starting a recording, the stimulation intensity was gradually increased until the participants felt a tugging sensation. The intensity level was then further increased until the participants felt that any additional increase would not be sensed, yielding the maximum tolerance level similar to previous studies.[7, 18, 19] This maximum tolerance level was used and recorded for all electrode pairs. In addition to NMES, the patients also performed conventional swallowing therapies or maneuvers such as chin tuck, multiple swallowing, effortful swallowing, supraglottic swallowing, Shaker's exercise, and the Mendelsohn maneuver depending on the clinical symptoms and VFSS findings. NMES and conventional therapies were given simultaneously by the same occupational therapist for each subject.

Outcome measures

Clinical and VFSS evaluations were performed before and after intervention within 1 week. The maximal duration between initial and follow-up evaluation was 4 weeks to minimize natural recovery. For clinical evaluations, MD Anderson dysphagia inventory (MDADI) was administered to assess quality of life in dysphagia and Likert scale (0–5) to measure satisfaction.[20]

For VFSS, subjects were seated upright in a neutral head position under a fluoroscopic machine. All fluoroscopic images of swallows were digitally recorded. Each VFSS was performed using the following boluses to swallow sequentially: extremely thick fluid (International dysphagia diet standardization initiative (IDDSI) 4); dysphagia I diet (IDDSI 4, pureed); dysphagia II diet (IDDSI 5, minced and moist); dysphagia III (IDDSI 7, regular); mildly thick (IDDSI 2); and thin fluid (IDDSI 0).[21] Each patient received an initial 3-mL bolus, followed by two 5-mL boluses. Fluids (thick, nectar-like, and thin) were delivered using 10-mL syringes; patients with dysphagia of grades I, II, or III were fed with spoons.

196 We analyzed the VFSS video using the videofluoroscopic dysphagia scale (VDS), functional oral
197 intake scale (FOIS) and PAS. VDS quantifies the severity of dysphagia; VDS is a 14-item scale
198 representing oral and pharyngeal functions that can be observed by VFSS.[22] PAS is an 8-point,
199 equal-appearing interval scale for describing any penetration and aspiration events.[16] By analyzing
200 these two scales, quantitatively analyzing the deglutition function is possible. All VFSS evaluations
201 were performed by two researchers in two groups who certified the modified barium swallow
202 impairment profile (MBSImP^{TM}). Thus, our results for each group are mean scores by two researchers.
203

204 ***Statistical analysis***

205 SPSS 21.0 software (SPSS Inc, Chicago, IL, USA) was used for all statistical analyses. Because the
206 number of patients is small, we used non-parametric statistics. The Wilcoxon signed-rank test was
207 used to compare the pretreatment and posttreatment evaluations. The Mann-Whitney test was used to
208 compare the differences of VFSS variables, VDS, and PAS variables between the 4- and 2-channel
209 NMES groups. The results are presented as the mean ± standard deviation. p values of less than 0.05
210 were considered statistically significant.

211

212 **Results**

213 A total of 26 participants (13 for 4-channel groups and 13 for 2-channel groups) were initially
214 enrolled; 1 participant in the 4-channel NMES group dropped out due to aggravated dizziness, and 2
215 participants dropped out due to too much sweating during NMES session and stoke aggravation.
216 Therefore, 12 participants in the 4-channel NMES group and 11 participants in the 2-channel NMES
217 group completed the clinical trial (Figure 2).

218 The demographic data of the participants are presented in Table 1. The average ages of the 4- and 2-

channel NMES group were 64.9 ± 16.5 years and 60.6 ± 14.2 years, respectively. The disease durations of the 4- and 2-channel NMES groups were 49.2 ± 109.1 and 32.6 ± 24.8 days, respectively. Initial VDS scores of the 4- and 2-channel groups were 63.6 ± 15.10 and 51.3 ± 15.7 and initial PAS scores were 5.7 ± 2.2 and 4.4 ± 2.7, respectively. In all areas examined before we started the NMES, both groups of pre-clinical trial evaluations showed no significant differences ($p > 0.05$) (Tables 1, 2).

In the comparison between before and after treatment, oral, pharyngeal, and total VDS scores were significantly improved in both groups ($p < 0.05$, Figure 3(A)). However, PAS and FOIS were significantly improved only in the 4-channel NMES group after treatment ($p < 0.05$, Figure 3(B)). Although subsets of MADI (emotional, functional, physical subsets) were significantly improved in the 4-channel NMES group, only emotional and physical subsets were significantly improved in the 2-channel NMES group (Table 2)

When we compared the changes of improvements between the two groups, oral VDS and total VDS score significantly improved in the 4-channel NMES group than in the 2-channel NMES group ($p < 0.05$). PAS and FOIS showed higher improvement in the 4-channel NMES group than in the 2-channel NMES group, but did not reach a significant level (p values of PAS and FOIS: 0.21 and 0.051, respectively). In MDADI, no significant difference was found between the two groups (Table 3).

Discussion

This is the first randomized, double-blind, parallel group, controlled trial that directly compared the rehabilitative effect of sequential 4-channel NMES with conventional 2-channel NMES. In the present study, clinical improvement was observed via sequential 4-channel NMES and 2-channel NMES in VDS. Only the sequential 4-channel NMES group showed significant improvement in PAS, FOIS, and subset of MDADI (functional) after treatment. When we directly compared the improvement between the two groups, the 4-channel group was superior to the 2-channel group in

oral and total VDS.

PAS improvement in sequential 4-channel NMES is a very important finding. Previous studies on 2-channel NMES showed conflicting results. Some studies have proven effectiveness, [23, 24] but others have shown no effect.[8, 25] The reason might depend on the application site and methods of NMES. In a previous study, NMES on submental placement alone does not change the PAS and National Institutes of Health-swallowing safety scale (NIH-SSS). However, submental and throat placements show a significant improvement in the NIH-SSS, but PAS is unchanged.[9] Two-channel NMES improves pharyngeal peristalsis and cricopharyngeal functions at the esophageal entry but does not affect the elevation of the hyolaryngeal complex, which has correlation with aspiration or penetration.[9, 13]

In a previous study that used 4-channel NMES by connecting two sets of 2-channel NMES suggested that the sequential 4-channel NMES facilitates the movement of hyolaryngeal structures during swallowing.[17] However, this system was made by combining two sets of 2-channel NMES; therefore, we could not adjust each channel. Thereby, we activated the first two channels for 1400 ms, then 300 ms later, and the third and fourth channels were activated for 1100 ms. The biggest difference from the previous study is that we stimulated the third channel, which is attached to the thyrohyoid muscle in 150 ms after stimulation of the first and second channels. A previous study evaluated during the effect, but the present study evaluated rehabilitative effect, which is commonly used for conventional 2-channel NMES.

The stimulation algorithm of sequential 4-channel NMES is based on normal contractile sequence. In the EMG analysis, the activations of the suprahyoid muscles developed about 150 ms and 350 ms earlier than those of the thyrohyoid and other infrahyoid muscles (sternohyoid and sternohyoid muscles). After 1400 ms of suprahyoid muscles' contraction, all of these muscles stop their contractions simultaneously.[10] These sequential contractions of the suprahyoid and infrahyoid

muscles accomplish the circular motion of the hyoid bone. The thyroid muscle assists laryngeal elevation, and other infrahyoid muscles, such as sternohyoid, sternothyroid, and omohyoid muscles, assist in prolonged laryngeal elevation and upper esophageal sphincter opening.[10, 26] This concept was verified by using kinematic and pressure analyses in a previous study.[17] Thus, the contractions of the thyrohyoid and other infrahyoid muscles, which have proper interval time with those of the suprahyoid muscles, may be important for dysphagia treatment, and our results verified the improvement of laryngeal complex for aspiration or penetration.[10]

The only muscle that elevates the larynx to the hyoid is the thyrohyoid muscle, which lies beneath the strap muscles, such as sternohyoid, sternothyroid, and omohyoid muscles.[9] In 2-channel NMES, simultaneous stimulation of submental and throat regions showed hyolaryngeal descent because sternohyoid and omohyoid stimulations exceeded the hyolaryngeal elevation effects. In other words, electrodes over the anterior neck might activate the sternohyoid and omohyoid rather than thyrohyoid and suprahyoid muscles. This hyolaryngeal descent is not a physiologic motion; therefore, the main mechanism of 2-channel NMES is strengthening of swallowing-related muscles.[27] However, theoretically, as 4-channel NMES uses normal contractile algorithm, the main mechanism of 4-channel NMES is not only strengthening of the supra and infrahyoid muscles but also increasing coordination of swallowing-related muscles.

In the present study, oral VDS and total VDS were significantly improved in the 4-channel NMES group compared with the 2-channel NMES group. Tongue-based pressure has been previously turned out to be important when the tongue comes in contact with the posterior pharyngeal wall, squeezing out the bolus through the pharynx.[28] Alterations in tongue coordination, strength, and pressure generation may result in a disruption of bolus movement from the oral cavity to the pharynx and result in increased risk of aspiration before or after swallowing.[29] Also, a previous study showed that a greater tongue strength results in a greater activation of the suprahyoid muscle during swallowing.[30] In the present study, one channel was attached to the suprahyoid muscles in 2-channel NMES, and the

first and second channels were attached to the bilateral suprahyoid muscles in 4-channel NMES. Considering that the effective depth of NMES is directly proportional to the distance between stimulation electrodes,[31] a wider placement of the coupled electrodes might more effectively stimulate not only the suprahyoid muscles but also the genioglossus or tongue muscles. Therefore, more channels and more covered lesion of the suprahyoid lesion in the sequential 4-channel NMES seem to induce effective contraction of the genioglossus and tongue muscles, which is highly correlated with tongue motion and is able to improve the strength of the tongue base, thereby resulting in superior efficacy in oral VDS scores.

In the present study, one participant in 2-channel NMES dropped out due to discomfort during NMES. In the 4-channel NMES group, aggravated dizziness was not related to NMES; therefore, no complication was developed. As sequential 4-channel NMES stimulated swallowing-related muscles with normal contractile algorithm, thereby inducing physiologic motion, less discomfort developed. Although the sample size was small and complication rate was negligible, 4-channel NMES is a safe and well-tolerated treatment method for dysphagia.

Originally, the purpose was to calculate the number of subjects in a future clinical trial to confirm the superiority of 4-channel NMES for future clinical trials. However, as 4-channel NMES sequentially stimulates swallowing-related muscles functionally and uses multi-channel for strengthening effect, our study verified the superiority of 4-channel NMES to 2-channel NMES with a small sample size. Follow-up study to verify the effectiveness of 4-channel NMES for pharyngeal phase is required.

This study has some limitations. First, a small number of subjects were included as this trial was a pilot study. As a result, pharyngeal VDS and FOIS were not significantly different between the two groups. However, the small number was enough to prove the superiority of 4-channel NMES in oral and total VDS. A follow-up study is required to verify the significant improvement of pharyngeal

VDS and FOIS. Second, treatment duration and daily sessions were different among the 5 rehabilitation units and general patients' condition. To manage this limitation, we did not use treatment frequency and time for the amount of NMES treatment, but used 420 min and 840 min as minimal and maximal treatment durations, respectively.

Conclusion

Compared with 2-channel NMES, sequential 4-channel NMES showed significant clinical improvement in PAS and VDS. It was superior to conventional 2-channel NMES, especially with respect to penetration or aspiration and oral function. PAS is important for dysphagic patients with regard to aspiration pneumonia and comorbidity. Sequential 4-channel NMES activating the suprahyoid, thyrohyoid, and other infrahyoid muscles with proper interval time is an effective treatment for dysphagia. It is a potentially effective treatment for dysphagia in patients with stroke. Further investigations involving larger population are needed to obtain better results.

Abbreviation

NMES: Neuromuscular electrical stimulation;
VFSS: videofluoroscopic swallowing study;
PAS: penetration-aspiration scale;
MDADI: MD Anderson dysphagia inventory;
IDDSI: International dysphagia diet standardization initiative;
VDS: videofluoroscopic dysphagia scale;
FOIS: functional oral intake scale;
NIH-SSS: National Institutes of Health-swallowing safety scale.

Declaration section

Ethics approval and consent to participate

The study protocol was approved by the institutional review board of each hospital (IRB No.: E-1806/475-002, 2018-07-012, JEJUNUH 2018-07-010, J-1810-064-979, DFH19DPOS033) and all methods were performed in accordance with the relevant guidelines and regulations. All patients or their representatives provided written informed consent prior to participation. It was also approved by the Ministry of Food and Drug Safety in Republic of Korea.

Consent for publication

Not applicable.

Availability of data and materials

All data in this study is available after de-identification upon reasonable request.

Competing interests

No commercial party having a direct financial interest in the results of the research supporting this article has or will confer a benefit upon the authors or upon any organization with which the authors are associated.

Funding

This research was supported by Basic Science Research Program through the National Research Foundation of Korea(NRF) funded by the Ministry of Science, ICT and Future Planning (NRF- NRF-2016R1D1A1B03935130)

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Acknowledgement

The authors gratefully appreciate MRCC team of Seoul National University Bundang Hospital for their work in the area of statistics in this study

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Figure 1. Locations of the electrode attachment. (A) Channel 1 (right) and channel 2 (left) electrodes were placed superior to the hyoid bone and posterior to the mandible with 1-cm interval from the midline, which were targeted for bilateral digastric and mylohyoid muscles. Channel 3 electrodes were placed on bilateral superior pole of the thyroid cartilage for the bilateral thyrohyoid muscles, and channel 4 electrodes were placed on medial to sternocleidomastoid muscles and inferior to the thyroid cartilage, which were targeted for the other infrahyoid muscles (sternohyoid, omohyoid, and sternothyroid muscles). (B) In 2-channel NMES system, channel 1 and 2 electrodes were attached to the suprahyoid and thyrohyoid muscles, respectively. Other electrodes were attached to the same location as 4-channel NMES system, but stimulations were only applied to channel 1 and 2 electrodes.

476 Figure 2. Flow of patients through the trial.

Figure 3. Comparison of improvements between pretreatment and posttreatment value in the 4-channel and 2-channel NMES groups. (A) Oral, pharyngeal, and total VDS scores were significantly improved in both groups ($p < 0.05$). (B) However, PAS and FOIS were significantly improved only in the 4-channel NMES group after treatment ($p < 0.05$).

Supplementary Figure 1. Sequential 4-channel NMES device. (A) The device has four channels that are adjustable for amplitude of current, latency, and duration of electrical stimulation. Sequential 4-channel NMES uses four pairs of electrodes for electrical stimulation. (B) The electrodes are round in shape and 22 mm in size. The gap between electrodes consists of two forms: 0.5 cm (type 1 electrode) and 1 cm (type 2 electrode). Type 1 electrode was used for channels 1, 2, and 4, and type 2 electrode was used for channel 3.