Effectiveness of Neuromuscular Electrical Stimulation on Dysphagia Treatment in Patients with Neurological Impairments – A Systematic Review and Meta-Analysis

Ruiying Ding1* and Fangchao Ma2

1Department of Communication Sciences & Disorders, Elmhurst College, USA
2Illinois Department of Public Health, Division of Patient Safety and Quality, USA

Abstract

Introduction: Studies that compared the use of neuromuscular electrical stimulation (NMES) with traditional dysphagia therapy (TDT) have been inconclusive. All previous meta-analysis studies have only used subjective measures to assess swallow function. The objective of the study is to perform a systematic review and meta-analysis evaluating the effectiveness of NMES for treatment of dysphagia associated with neurological impairment utilizing both subjective measures of swallows function and objective measures such as penetration-aspiration scale and pharyngeal transit time (PTT).

Methods: A systematic search of PUBMED, Cochrane Central Register of Controlled Trials, EMBASE and Google Scholar between 1 January 2001 to 31 March, 2016 was conducted to identify all relevant articles that compared NMES versus TDT for treatment of adult patients with acute neurological impairments, mainly stroke and brain injury. A total of 12 studies were included in the study. Relevant data were extracted and the standardized mean difference (SMD) is used as summary statistics.

Results: The pooled SMD revealed that NMES group showed significant improvement in swallowing function 1-3 month post treatment as compared to TDT group (SMD=1.14, 95% CI: 0.94-1.34, p<0.001), in reduction of penetration/aspiration (SMD=-0.85, 95% CI: -1.17 - -0.52, p<0.001), and in reduction of PTT (SMD=-0.86, 95% CI: -1.17- -0.55, p<0.001).

Conclusion: The present meta-analysis finds NMES is an effective adjunct modality to TDT for patients suffering from stroke and traumatic brain injury.

ABBREVIATIONS

NMES: Neuromuscular Electrical Stimulation; TDT: Traditional Dysphagia Therapy

INTRODUCTION

Dysphagia is a common functional impairment during the acute phase of neurological impairment after suffering a stroke or severe traumatic brain injury (TBI) [1]. Dysphagia occurs in 22% to 70% of patients with stroke and 38% to 65% in TBI [2], depending on the timing of the assessment, diagnostic methods and criteria [3,4]. Although many patients recover from stroke or TBI related dysphagia within 2 weeks post onset [5,6], it has been reported that up to 50% of patients demonstrate persistent swallowing difficulty six months poststroke [3]. Twenty three percent of patients with TBI still present aspiration one year post incident [4]. Persistent dysphagia increases the risk of malnutrition, dehydration, and aspiration pneumonia in these populations [7]. Dysphagia is associated with increased mortality, higher dependence on tube feeding, and extended hospitalization [8]. To reduce dysphagia associated morbidity and mortality and return patients to the most optimal diet possible to improve their quality of life, effective treatment of dysphagia is extremely important [9].

Traditional approaches to alleviate dysphagia and mitigate the negative impact thereof are based on a variety of behavioral treatments and environmental and diet modifications. Effective management of dysphagia involves a combination of diet modification, position adjustments, and swallowing maneuvers to enhance swallow efficiency and airway protection during swallowing [9]. Within a traditional treatment paradigm, techniques may focus on the use of oral motor exercises, maneuvers, postural changes, and increasing sensory awareness [10]. More recently, several adjunctive treatment options became available to improve dysphagia recovery. One such a treatment...
modality is neuromuscular electrical stimulation (NMES), which has
been received with great interest by speech-language pathologists
NMES as treatment modality for dysphagia involves the application
of an electrical current to peripheral tissue targets. Such stimulation
aims to improve swallow function by strengthening the swallowing
musculature or by stimulating the sensory pathways relevant to
swallowing, or both [12].

A number of studies that compared the use of NMES with
traditional treatment techniques have been inconclusive [13-
15]. A preliminary meta-analysis conducted by Carnaby-Mann
and Crary [13] investigated the effectiveness of NMES compared
to TDT using subjective swallow score and revealed a small but
significant summary effect size for transcutaneous NMES for
swallowing. A 2013 meta-analysis has shown that NMES is more
effective in treatment of adult dysphagia of variable etiologies,
than traditional therapies, but a subgroup analysis of post-
stroke patients has not shown any difference between the two
modalities [15]. More recently, Chen et al. [14], have reported
that traditional treatment combined with NMES seems to be more
effective in treating dysphagia than traditional therapy alone for
patients with stroke in the short term. However, they reported
a significant heterogeneity of studies included in their meta-
analysis, which led to reduced generalizability of their results.
All the meta-analysis studies to date have used only subjective
measurements such as Functional Oral Intake Scale (FOIS) as the
indicator of improvement in swallow function post NMES, none
has performed meta-analysis for objective measures derived
from video fluoroscopy or Fiberoptic Endoscopic Evaluation of
Swallowing (FEES) [13-15]. In both stroke and TBI, the symptoms
of dysphagia were most severe at the onset of the disease and
some spontaneous recovery is expected in the acute phase of
the disease [6]. The current meta-analysis assesses the efficacy
of NMES in dysphagia treatment secondary to neurological
impairments caused by stroke and TBI. The current meta-analysis
will assess both subjective and objective outcome measures in
the investigation of the effectiveness of NMES in patients with the
neurological damage. The findings from this study should guide
evidence-based clinical decision making on the use of NMES for
treating dysphagia in patients with neurological impairments.

MATERIALS AND METHODS

Study selection

A systematic search was conducted to identify all relevant
articles published between 1 Jan, 2001 to 31 March 2016.
The year 2001 was chosen because the first NMES study was
published by Freed et al. in 2001 [16], even though the study
was criticized for selective treatment group assignments. The
search was conducted in PubMed, Cochrane Central Register of
Controlled Trials, EMBASE, and Google Scholar. The following
key search terms were used: stroke, dysphagia, neuromuscular
electrical stimulation, NMES, neurological impairment, brain
injury, swallow dysfunction. These search terms were used in
various combinations to yield maximized results yet maintain
sensitivity and specificity. Citation tracking of all selected article
references was also conducted.

Two researchers independently searched the electronic
databases for relevant articles and evaluated the articles. Initial
evaluation was based on an inclusion strategy that was built on
etiology of dysphagia in participants, study type, intervention
type, and outcome measures. The article title and abstract was
first reviewed using the above-mentioned strategy, if relevant,
the full text was reviewed. The following criteria were used
for inclusion in the present analysis: 1) randomized clinical
trials or quasi-experimental studies published in the English
language that compared NMES versus TDT for treatment of adult
patients with acute neurological impairments, mainly stroke
and traumatic brain injury; 2) The NMES intervention was placed
on the surface of the neck or submental area; 3) a validated
outcome measurement on swallow function was available. A consensus
between the two reviewers ensured that the studies met the
criteria for inclusion. The evaluation and selection process is
summarized in Figure (1).

Data extraction

Studies that met the inclusion criteria were thoroughly
reviewed and the following data were extracted from each
article, 1) details of the study design and sample size; 2) patient
characteristics, both demographic (age, gender) and clinical
(stroke or brain injury location and time since onset); 3) treatment
procedures including NMES frequency and duration and types of
traditional therapy; 4) outcome measures; and 5) assessment
interval. One of the limitations in reviewing these studies is the
lack of a uniform measurement to assess swallow function [13].
Therefore, a mixture of outcome measures was included in the
present analysis. For subjective measures of swallow function,
Functional Oral Intake Scale (FOIS) were most commonly used
and it has been validated and has shown strong reliability and
validity in acute stroke patients [17]. The FOIS evaluates the
safe ingesting food/liquids by mouth based on patient report.
The FOIS ranges from Level 1 which is ‘nothing by mouth’ to
Level 7 ‘total oral diet with no restriction’. The FOIS were used
in six of the selected twelve studies [1,8,18-21]. Therefore it was

Figure 1 Flow Chart of the Selection Process for the Inclusion or
Exclusion of Studies.
chosen for estimate of effect size. In the studies that FOIS was not used, a measuring scale of swallowing function similar to FOIS were used to estimate effect size, such as the American Speech-Language-Hearing Association National Outcome Measurement System (ASHA NOMS) [22], Swallowing score [16], Standardized Swallowing Scale (SSA) [23], and the Visual Analog Scale (VAS) [24]. The above mentioned scales were chosen to calculate standardized mean differences (SMD).

Studies that included objective measures of swallow function were analyzed separately. The most commonly used objective measures are the PAS [18,20,22] and the PTT [1,22,23,25]. These objective measurements are derived from two common instrumentation methods in the evaluation of swallowing: video fluoroscopy and fiberoptic endoscopic evaluation of swallowing (FEES). Video fluoroscopy is a moving X-ray study that can visualize oral, pharyngeal and esophageal phases of swallowing and provide complete and objective assessment of swallowing timing, residue and presence of aspiration and is considered a gold standard in the evaluation of swallowing [5]. FEES is a newer reliable and valuable technique that can be used to assess pharyngeal dysphagia, determine aspiration and guide treatment by visualizing the pharyngeal structures and related events during the pharyngeal phase of swallowing.

The most commonly used measurement that assessed the presence of penetration/aspiration is the PAS. It divides the condition of aspiration into eight levels. This measurement corresponds directly with laryngeal closure or laryngeal vestibule closure during the pharyngeal phase of the swallow. Two studies used other scales that included items describing the status of aspiration and penetration, e.g., video fluoroscopic dysphagia scale (VDS) [21,26]. The scale includes 14 items that represent the oral and pharyngeal function, including the penetration and aspiration observed in the video fluoroscopic study. A study by Bulow et al. used a scale that rated “misdirection swallow” to represent aspiration of food [24]. All studies that included measures that assessed the presence of penetration/aspiration were included in the meta-analysis.

The second objective measure PTT, was defined as the interval (in sec) between the first frame showing the arrival of the bolus head at the cross point of tongue base and the lower rim of the mandible and the last frame showing the tail of the bolus passing through the upper esophageal sphincter. It was related to the speediness of the pharyngeal phase of the swallow. Studies that included the PTT were analyzed separately in the meta-analysis.

In all the selected studies, sample size, mean difference between baseline and post-treatment, and standard deviation of the difference for selected outcome measures were extracted from experimental and control groups. When an outcome was measured in multiple intervals, the first post-treatment measure was used. If a study reported medians and inter quartile ranges (or range) instead of means and standard deviations (SDs), the means and SDs were imputed using the methods described by Hozo et al. [27]. For studies in which standard deviations for changes from baseline were not reported, SDs were imputed based on the method proposed by Cohen [28].

Statistical analysis

The standardized mean difference (SMD) also known as Cohen’s d is used as a summary statistic in this meta-analysis. As most of the selected studies are quasi-experimental trials lacking randomization, SMDs were calculated on the mean differences between post-treatment and baseline. SMD is often used for continuous measures when the studies all assess the same outcome but measure it in different scales. In the present study, meta-analysis was performed separately for studies using subjective measures and for studies using objective measures. A SMD less than 0.5 are considered small, between 0.5 and 0.8 medium, and greater than 0.8 large. SMD of medium or above is considered clinically meaningful [28].

Since all studies used an analogous metric of treatment effectiveness, a fixed-effect model was used. Because all the included studies are not comparable in terms of interventions and outcomes, it is likely there is variation across studies, and this variation is estimated by heterogeneity. Cochran’s Q is used to test if there is significant heterogeneity and F and chi-square tests were used to measure the degree of inconsistency in the studies’ results [29]. An F score > 50% indicated significant heterogeneity. In the present study, analyses were performed using the SAS 9.3 for Windows (www.sas.com) and MedCalc Statistical Software version 15.10.0 (MedCalc Software bvba, Ostend, Belgium), and the statistical significance level was set at 0.05.

RESULTS

A total of 12 studies were included in the meta-analysis based on the inclusion criteria [1,8,16,18-26]. These studies were either randomized clinical trials or quasi-experimental trials and quantifiable measures of swallowing function could be extracted. Many earlier studies were excluded because of their before-after design that lacked controls.

Characteristics of included studies, interventions, and outcome measures

Information on study authors and published year, sample size, age of the patients, neurological impairment, time since onset, study design, NMES frequency and duration, types of TDT, and assessment interval is summarized in Table (1) with studies listed chronologically by publication year. Among the 12 studies included in the present analysis, 8 were randomized clinical trials (Study # 2, 3, 4, 7, 8, 9, 10, 12) and the other 4 studies were quasi-experimental trials (Study # 1, 5, 6 and 11), with a combined study population of 578 stroke or TBI patients suffering from moderate to severe dysphagia. NMES groups consisted of 344 patients versus 234 controls that were treated with TDT which included posture and diet changes, oral motor exercises, and thermal-tactile stimulation and / or swallow maneuvers. Study # 5 and 12 consisted of both stroke and TBI patients, and the rest included only stroke patients. Four studies exclusively focused on stroke in hemispheric region (Study # 2, 9, 10, and 11), one on stroke in supratentorial region (Study #B), the remaining studies consisted of multi-location strokes. More than half of the studies investigated the effect of NMES on dysphagia treatment in the acute phase of stroke or TBI (Study # 4, 5, 6, 7, 8, 10).
Table 1: Summary of the studies included in the meta-analysis.

<table>
<thead>
<tr>
<th>Study</th>
<th>Authors &amp; year</th>
<th>Age (years)</th>
<th>Sample size (NMES/TDT)</th>
<th>Diagnoses (Location)</th>
<th>Time since onset</th>
<th>Study design (Intervention type)</th>
<th>Traditional Therapy</th>
<th>NMES Frequency/Duration</th>
<th>Assessment interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Freed et al. 2001</td>
<td>75.7/78.1</td>
<td>99 (63/36)</td>
<td>stroke (brainstem, hemispheric, multiple strokes)</td>
<td>not reported</td>
<td>quasi-experimental (NMES vs TDT)</td>
<td>TTS</td>
<td>in-patients 1h/day out-patients 1h/day 3d/week until swallow score of 6 or no more progress</td>
<td>0 and final Follow-up time up to 3 years</td>
</tr>
<tr>
<td>2</td>
<td>Bulow et al. 2008</td>
<td>70.0/71.0</td>
<td>25 (12/13)</td>
<td>stroke (hemispheric)</td>
<td>&gt;3 month</td>
<td>randomized trial (NMES vs TDT)</td>
<td>diet modification, exercises</td>
<td>1-hour session, 5 sessions a week, for 3 weeks</td>
<td>0 and 3 weeks</td>
</tr>
<tr>
<td>3</td>
<td>Lim et al. 2009</td>
<td>67.8± 8.1/ 60.8±12.3</td>
<td>28 (16/12)</td>
<td>infarction, hemorrhage (hemisphere, subarachnoid)</td>
<td>13 &lt; 6 months, 3 &gt;6 months/9 &lt;6 months, 3 &gt;6 months</td>
<td>randomized trial (NMES +TDT vs TDT)</td>
<td>TTS</td>
<td>1-hour sessions, 5 sessions a week, for 4 weeks</td>
<td>0 and 4 weeks</td>
</tr>
<tr>
<td>4</td>
<td>Permsirivanchich et al. 2009</td>
<td>64.5±8.8/ 64.3±9.4</td>
<td>23 (12/11)</td>
<td>stroke</td>
<td>average 24 days</td>
<td>randomized trial (NMES vs TDT)</td>
<td>Compensatory, exercises, maneuvers</td>
<td>1-hour session, 5 sessions a week, for 4 weeks</td>
<td>0 and 4 weeks</td>
</tr>
<tr>
<td>5</td>
<td>Beom et al. 2011</td>
<td>66.1±9.5/ 68.5±12.5</td>
<td>28 (7/21)</td>
<td>stroke and TBI (Cortex, subcortex, brainstem)</td>
<td>2.4±2.1/ 1.3±1.0 (months)</td>
<td>quasi-experimental (NMES+ TDT vs TDT)</td>
<td>Compensatory, exercises, maneuvers, and TTS</td>
<td>30-minute sessions, 5 sessions a week, for 4 weeks</td>
<td>0 and 4 weeks</td>
</tr>
<tr>
<td>6</td>
<td>Kushner et al. 2013</td>
<td>19-89 (range)/ 49-91</td>
<td>92 (65/27)</td>
<td>stroke (hemispheric, intracerebral hemorrhage, brainstem)</td>
<td>&lt;16 days</td>
<td>quasi-experimental (NMES+ TDT vs TDT)</td>
<td>Compensatory, exercises, maneuvers, and TTS</td>
<td>1-hour session, 5-6 sessions a week, for an average of 18 days</td>
<td>0 and averaged 18 days (SD=3)</td>
</tr>
<tr>
<td>7</td>
<td>Huang et al. 2014</td>
<td>68.9±9.8/ 64.5±14.4/ 67.0±10.1</td>
<td>29 (10/8/9)</td>
<td>Stroke (hemispheric)</td>
<td>&lt;3 months</td>
<td>randomized trial (NMES+ TDT vs NMES vs TDT)</td>
<td>Compensatory, exercises, maneuvers, and TTS</td>
<td>1-hour session, 3 sessions a week, for 10 sessions</td>
<td>0 and 3 weeks</td>
</tr>
<tr>
<td>8</td>
<td>Lee et al. 2014</td>
<td>63.4±11.4/ 66.7±9.5</td>
<td>57 (31/26)</td>
<td>ischemic stroke (supratentorial)</td>
<td>10 days or less</td>
<td>randomized trial (NMES+ TDT vs TDT)</td>
<td>exercises, maneuvers, and TTS</td>
<td>30-minute sessions, 5 sessions a week, for 3 weeks</td>
<td>0,3, 6, 12 weeks</td>
</tr>
<tr>
<td>9</td>
<td>Li et al. 2014</td>
<td>66.7±14.6/ 65.8±13.2/ 66.4±13.1</td>
<td>118 (40/38/40)</td>
<td>stroke (hemispheric)</td>
<td>&gt;3 months</td>
<td>randomized trial (NMES+ TDT vs NMES vs TDT)</td>
<td>compensatory and exercises</td>
<td>1-hour session, 5 sessions a week, for 4 weeks</td>
<td>0 and 4 weeks</td>
</tr>
<tr>
<td>10</td>
<td>Lim et al. 2014</td>
<td>66.3±15.4/ 62.5±8.2</td>
<td>33 (18/15)</td>
<td>stroke (hemispheric)</td>
<td>&lt;3 months</td>
<td>randomized trial (NMES+ TDT vs TDT)</td>
<td>Compensatory, exercises, maneuvers and TTS</td>
<td>30-minute session, 5 sessions a week, for 2 weeks</td>
<td>0, 2, 4 weeks</td>
</tr>
<tr>
<td>11</td>
<td>Toyama et al. 2014</td>
<td>63.6 ± 21.4/ 67.2 ± 13.7</td>
<td>26 (12/14)</td>
<td>brain injury (hemispheric)</td>
<td>25.2 ± 25.9/14.7 ± 10.6 (weeks)</td>
<td>quasi-experimental (NMES+ TDT vs TDT)</td>
<td>TTS with dry swallow</td>
<td>40-min sessions, 5 days per week, for 8 weeks</td>
<td>0, 8 weeks</td>
</tr>
<tr>
<td>12</td>
<td>Terre et al. 2015</td>
<td>46/51</td>
<td>20 (10/10)</td>
<td>stroke and traumatic brain injury</td>
<td>subacute</td>
<td>randomized trial (NMES+ TDT vs TDT)</td>
<td>diet change, exercises and maneuvers</td>
<td>1-hour session, 5 sessions a week, for 4 weeks</td>
<td>0, 4 weeks, 3 months</td>
</tr>
</tbody>
</table>

**Abbreviations:** NMES: Neuromuscular Electrical Stimulation; TDT: Traditional Dysphagia Therapy
Various intervention schemes or combination of therapies were employed in the included studies. Earlier studies (Study # 1, 2, 4) centered the attention on the effectiveness of NMES alone for treatment of dysphagia, while more recent studies focused investigation on the efficacy of traditional swallow therapy plus NMES for treatment of dysphagia following stroke or TBI. In the majority of the studies, types of TDT included a combination of compensatory strategies, thermal-tactile stimulation, exercises and maneuvers (Study #2, 4, 5, 6, 7, 8, 9, 10, 12). Only three studies (Study #1, 3, 11) used thermal-tactile stimulation as the only type of TDT. In most of the studies, NMES intensity on patient’s tolerance usually set the intensity level at the point when a patient felt pain or discomfort; only in study # 9 and 10, a relative low-intensity of 7-9 mA was used which was sufficient to induce tingling sensation. Few studies evaluated the long term effects of NMES. Only Study # 1 8, 12 followed the patients for 3 months or longer. Therefore this analysis focused on examining the short-term effects of NMES, which were demonstrated in the changes of subjective and objective outcome measures between baseline and immediate post treatment.

Standardized mean differences of swallowing function scores

A mixture of outcome measures were used in the studies included in the present analysis. FOIS was used most often and was used in half of the selected 12 studies [1,8,18-21]. Therefore FOIS data was chosen to estimate the effect size. In the studies that FOIS was not used, a measuring scale of swallowing function similar to FOIS would be chosen for estimating effect size, such as ASHA NOMS [22], Swallowing score [16], SSA [23], and VAS [24]. The aforementioned scales were used to calculate SMD. Results of meta-analysis of swallowing function scores are shown in Table (2) and the effect sizes of individual studies and overall SMD are shown in a forest plot (Figure 2). For subjective swallow measures, the pooled SMD using a fixed-effect model revealed that NMES group showed significant improvement in swallowing function post treatment as compared with TDT group (pooled SMD = 1.14, 95% CI: 0.94-1.34, p < 0.001). The Heterogeneity was significant, indicating inconsistency among the selected studies’ results (I 2 = 81%, 95% CI: 66%-89%).

For objective swallow measures that investigate the presence of aspiration and penetration, PAS was used in 3 of the 6 studies [18,20,22]. Two of the 6 studies used VDS [21,26] and one study used “misdirection swallow” that also described the presence of aspiration and penetration [24]. The results are shown in Table (3) and the forest plot in Figure (3). Similarly, the pooled SMD showed significantly reduced occurrence of penetration/aspiration in NMES group as compared to the control group (pooled SMD = -0.85, 95% CI: -1.17 - -0.52, p < 0.001). However, high heterogeneity was shown (I 2 = 89.87%, 95% CI: 81%-95%).

For objective measures that investigate the speed of pharyngeal phase, PTT was used in 4 out of the 12 studies [1,22,23,25]. The results are shown in Table (4) and the forest plot in Figure (4). The pooled SMD revealed that NMES group showed significantly reduced PTT post treatment as compared with TDT group (pooled SMD = -0.86, 95% CI: -1.17 - -0.55, p < 0.001).

Table 2: Normalized mean difference of subjective swallowing function changes post-treatment from baseline.

<table>
<thead>
<tr>
<th>Source</th>
<th>Measurement*</th>
<th>NMES</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Freed et al., 2001</td>
<td>Swallow score</td>
<td>63</td>
<td>3.76</td>
</tr>
<tr>
<td>Bulow et al., 2008</td>
<td>VAS</td>
<td>12</td>
<td>2.90</td>
</tr>
<tr>
<td>Permsirivanich et al, 2009</td>
<td>FOIS</td>
<td>12</td>
<td>3.17</td>
</tr>
<tr>
<td>Toyama et al., 2013</td>
<td>FOIS</td>
<td>12</td>
<td>1.40</td>
</tr>
<tr>
<td>Kushner et al., 2013</td>
<td>FOIS</td>
<td>65</td>
<td>4.40</td>
</tr>
<tr>
<td>Huang et al., 2014</td>
<td>FOIS</td>
<td>10</td>
<td>3.70</td>
</tr>
<tr>
<td>Lee et al., 2014</td>
<td>FOIS</td>
<td>31</td>
<td>1.40</td>
</tr>
<tr>
<td>Lim et al., 2014</td>
<td>ASHA NOMS</td>
<td>18</td>
<td>1.10</td>
</tr>
<tr>
<td>Li et al., 2015</td>
<td>SSA</td>
<td>45</td>
<td>17.70</td>
</tr>
<tr>
<td>Terre et al., 2015</td>
<td>FOIS</td>
<td>10</td>
<td>2.60</td>
</tr>
<tr>
<td>Total (fixed effects)</td>
<td></td>
<td>278</td>
<td></td>
</tr>
</tbody>
</table>

Test for heterogeneity

| Q | 46.9251 |
| DF | 9 |
| Significance level | P < 0.0001 |
| I 2 (inconsistency) | 80.82% |
| 95% CI for I 2 | 65.69 to 89.28 |

Figure 2 Forest plot of effect sizes for the studies with measures FOIS/VAS/SSA/Swallow Score/ASHA-NOMS*

Table 3: Standardized mean difference of penetration/aspiration changes post-treatment from baseline.

<table>
<thead>
<tr>
<th>Source</th>
<th>Outcome measurement used in analysis*</th>
<th>Experimental</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Mean change posttreatment from baseline</td>
<td>SD</td>
</tr>
<tr>
<td>Bulow et al., 2008</td>
<td>Misdirection</td>
<td>12</td>
<td>-0.58</td>
</tr>
<tr>
<td>Beom et al., 2010</td>
<td>VDS</td>
<td>7</td>
<td>-11.90</td>
</tr>
<tr>
<td>Toyama et al., 2013</td>
<td>VDS</td>
<td>12</td>
<td>-21.40</td>
</tr>
<tr>
<td>Lim et al., 2014</td>
<td>PAS</td>
<td>20</td>
<td>-2.63</td>
</tr>
<tr>
<td>Huang et al., 2014</td>
<td>PAS</td>
<td>8</td>
<td>-1.30</td>
</tr>
<tr>
<td>Lee et al., 2016</td>
<td>PAS</td>
<td>25</td>
<td>-1.36</td>
</tr>
<tr>
<td>Total (fixed effects)</td>
<td>84</td>
<td>102</td>
<td>-0.845</td>
</tr>
</tbody>
</table>

Test for heterogeneity
- $Q = 49.3809$
- $DF = 5$
- Significance level $P < 0.0001$
- $I^2$ inconsistency = 89.87%
- 95% CI for $I^2$ = 80.66 to 94.70

Abbreviations: VDS: Videofluoroscopic Dysphagia Scale; PAS: Penetration-Aspiration Scale

DISCUSSION

In patients with neurological impairment such as stroke or TBI, dysphagia can result from loss of voluntary control of the muscles involved in swallowing due to muscle weakness or atrophy from disuse or long-term tube feeding [18,19,26,30]. Stroke and TBI patients can also demonstrate reduced oropharyngeal sensation and delayed timing in triggering the pharyngeal swallow which could lead to aspiration [31]. NMES used as an adjunct modality in the treatment of dysphagia has gained popularity in the recent years [13]. There are several hypotheses on the mechanism of NMES in treatment of dysphagia. NMES does not cause muscle contraction, rather it selectively recruits motor units and increases muscle strength and targets healthy innervated muscle fibers and facilitates muscle contraction during functional...
activities [13]. NMES can also recruit more motor units than volitional contraction and may produce greater muscle strength gains than exercise alone [32]. It is postulated that NMES can improve both motor and sensory aspects of swallowing by improving hyolaryngeal elevation, restoring motor function of weak muscles, combating disuse atrophy, enhancing sensory awareness, and facilitating muscle contraction [33,34]. It has been reported that NMES administered during execution of a purposely motor task may be superior to NMES administered when the target muscle is at rest [31,35] which may explain why NMES works better when combined with TDT.

Previous meta-analysis of the effectiveness of NMES in patients with dysphagia has shown promising results. Patients have shown improvement in swallow function as reflected in upgraded diet consistencies [13-15]. In previous meta-analyses, either neurological impairment was not singled out for analysis [13] or an insignificant association was reported [15]. The current study is the only meta-analysis investigating the effectiveness of NMES using both subjective and objective measures to assess swallow function. The current study found that NMES combined with TDT was more effective than TDT alone in dysphagia treatment in patients with stroke and TBI, particularly for patients with stroke in the acute phase. In addition to subjective measure of swallow function, the current study also investigated...

Table 4: Standardized mean difference of pharyngeal transit time changes post-treatment from baseline.

<table>
<thead>
<tr>
<th>Source</th>
<th>Outcome measurement used in analysis</th>
<th>Experimental</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Mean change posttreatment from baseline</td>
<td>SD</td>
</tr>
<tr>
<td>Lim et al., 2009</td>
<td>PTT (liquid)</td>
<td>16</td>
<td>-0.10</td>
</tr>
<tr>
<td>Lim et al., 2014</td>
<td>PTT (liquid)</td>
<td>20</td>
<td>-0.06</td>
</tr>
<tr>
<td>Li et al., 2015</td>
<td>PTT (liquid)</td>
<td>45</td>
<td>-0.10</td>
</tr>
<tr>
<td>Torre et al., 2015</td>
<td>PTT</td>
<td>10</td>
<td>0.11</td>
</tr>
<tr>
<td>Total (fixed effects)</td>
<td>91</td>
<td>87</td>
<td>-0.856</td>
</tr>
</tbody>
</table>

Test for heterogeneity

| Q       | 13.3141 |
| DF | 3 |
| Significance level | P = 0.0040 |
| I² (inconsistency) | 77.47% |
| 95% CI for I² | 38.82 to 91.70 |

**Abbreviations**: PTT: Pharyngeal Transit Time
the effectiveness of NMES using objective measures that investigate the presence of aspiration/penetration and the speed of pharyngeal phase. The study showed significant improvement in both measures in patients who received NMES and TDT as compared to TDT alone. The improvement in swallow function was reflected not only in improvement of diet consistency and/or method of intake (e.g. from nothing by mouth to soft diet), but also in reduction of penetration and/or aspiration as well as PTT.

NMES stimulates the suprathyroid muscle group resulting in improved elevation of the hyoid bone and the laryngeal system, which restores the function of the protective mechanism of the airway and the opening of the upper esophageal sphincter. Increased laryngeal elevation and airway closure contribute to reduced penetration and aspiration in patients. NMES also improves the sensory and motor aspects of the swallow function which subsequently improve the coordination of the pharyngeal phase of the swallow as demonstrated by reduction in PTT in this meta-analysis.

Systematic reviews and meta-analyses can provide convincing and reliable evidence relevant to many aspects of medicine and health care [36]. Such studies are especially valuable when the results of the studies included in the meta-analyses show clinically important effects of similar magnitude (homogeneity). However, the conclusions are less clear when the included studies have differing results as in the case of a significant heterogeneity [29]. Consistent with previous meta-analysis, our current study also showed large heterogeneity in the three measures: swallow function, presence of penetration-aspiration and PTT [13-15]. Since multiple outcome measures were used in the studies included in the meta-analysis, it is inevitable that heterogeneity was a problem which may reduce the clinical value of the studies.

The present study has several limitations and the study findings should be interpreted with caution. As with any meta-analysis, this study cannot address the problems in the original studies, which include study design flaws, inappropriate statistical methods, and incomplete presentation of some of the results. Some of the studies included in the analysis were quasi-experimental trials, lacking randomization, and differed significantly in patient population characteristics. Lack of a standardized NMES treatment protocol is problematic as treatment intensity, frequency and duration varied among the studies. Outcome measures were observed by un-blinded researchers/data collectors which may subject to observation bias [13-15]. In addition, this analysis used SMD method in which the overall intervention effect can also be difficult to interpret as it was reported in units of standard deviation rather than in units of any of the measurement scales used in the review. Despite these limitations, the present analysis included the largest number of studies to date for a meta-analysis of NMES in dysphagia treatment and was the first systematic review of the effectiveness of NMES in patients with neurological impairments and the only one that included both subjective and objective measures to assess swallow function.

The present study only evaluated the short-term effects of NMES in dysphagia treatment in patients with acute neurological impairment as treatment data from more than 3 months are scarce. Oh et al. [37], has proposed that NMES can show long lasting effects of improvement via cortical reorganization as studies have shown cortical representation areas can be modified by sensory and motor stimulation. Few studies have examined the long-term effects of NMES in patients with oropharyngeal dysphagia secondary to acquired brain injury. One of the studies included in the present study did find that the most significant reduction in aspiration occurred between 3 and 6 months, supporting the hypothesis that NMES accelerates the recovery
process in stroke and TBI patients (1). Sun et al. [31], have reported a persistent and significant long-term effect of NMES on stroke-related dysphagia. They observed that at 2-year follow-up, 15 of the 21 (71.4%) initial tube-fed patients improved enough to no longer require a feeding tube, and the majority (79.3%) of patients maintained an oral diet with no pulmonary complications. These preliminary data suggests positive long-term effects of NMES in dysphagia treatment in patients with acute neurological impairments such as stroke and TBI.

CONCLUSION

The present meta-analysis has found that NMES as an adjunct therapy is more effective for the treatment of dysphagia secondary to neurological impairments than using the traditional therapy alone. The effect was especially convincing with patients in the acute phase of stroke. Future large scale randomized clinical trials among this patient population with objective measures quantifying the effect size and long-term follow-up is warranted. In addition, variability in duration and intensity measures quantifying the effect size and long-term follow-up is warranted. Dysphagia affects more than half of the patients with acute neurological impairments such as stroke or TBI [2-4], any improvement in the effectiveness of the treatment regimen would lead to reduced complications, better quality of life for the patients, and decreased mortality rates. The present findings should provide evidence based clinical practice guidelines in utilizing NMES as an effective adjunct modality to the traditional therapy for stroke and TBI patients suffering from dysphagia.

CONFLICT OF INTEREST

The authors Ruiying Ding and Fangchao Ma certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers’ bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

REFERENCES

23. Li L, Li Y, Huang R, Yin J, Shen Y, Shi J. The value of adding transcutaneous neuromuscular electrical stimulation (VitalStim) to traditional


