

## Impact of Dysphagia Therapy in Parkinson's Disease

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### ABSTRACT

**Background:** Dysphagia is a common symptom in Parkinson's disease (PD) which indicates a difficulty in swallowing. It has been accompanied with poor quality of life (QoL), anxiety and depression.

**Aim of the Study:** to assess the effects of dysphagia treatment in Parkinson's disease.

**Materials and methods:** Studies published up to July 2017 were found via a systematic comprehensive electronic database search using PubMed, Embase, and The Cochrane Library. Two reviewers independently assessed the studies using strict inclusion criteria. **Results:** Thirteen studies were enrolled in the present study and qualitatively analyzed using critical appraisal items. The review includes rehabilitative (exercises, electrical stimulation, bolus modification etc.) and pharmacologic treatment. Some well-designed controlled trials were included. However, none of the included studies fulfilled all criteria for external and internal validity. Thus, a meta-analysis was not carried out as most of the studies were not of sufficient quality. **Conclusion:** Rehabilitative treatment including Expiratory Muscle Strength Training (EMST) may be effective for dysphagia treatment solely coupled with dopaminergic therapy for PD. Recently developed other treatment methods such as implant-prosthetic treatment and percutaneous injection of botulinum neurotoxin type A in the cricopharyngeal muscle on dysphagia is rather promising. Nevertheless, these preliminary results warrant further investigation concerning their clinical applicability, and further research should be conducted.

**Keywords:** Dysphagia; Swallowing disorder, Parkinson's disease, Therapy outcome.

### INTRODUCTION

Parkinson's Disease (PD) can lead to problems with swallowing in between 31%-100% of individuals, at any time during disease<sup>[1]</sup>. Normally, the disturbance is linked with bulbar structure dysfunction affecting movements, with possible tongue tremor, food bolus flow weakening, prolonged time during bolus transit, delayed swallowing reflex, poor palate elevation, weakening of epiglottis motility, regurgitation, tracheal penetration and aspiration<sup>[2]</sup>. Despite all these clinical symptoms, a parkinsonian individual's initial alterations in swallowing – also called dysphagia – are normally undetected. By the time the patient starts worrying about swallowing difficulties, frequently dysphagia is already in an advanced stage<sup>[3]</sup>. with a functional decline able to critically damage quality of life (QL). Thus, an early swallowing functioning assessment in PD is necessary, as well as measuring its impact on quality of life, to promote better results from the use of therapeutic resources and optimize treatment.

Moreover, studies showed that pneumonia is the main cause of death in patients with

PD, demonstrating the importance of speech-language pathologist (SLP)-based intervention for dysphagia to delay the onset of this symptom<sup>[4]</sup>. Within this context, a growing number of studies have been collected to assess the efficacy and efficiency of therapeutic interventions made by SLP for this signs and symptom of dysphagia in PD, as described above<sup>[5]</sup>. These studies have demonstrated the benefits of several treatment strategies in decreasing signs and symptoms of dysphagia and improving swallow safety in patients with PD, including food consistency modification, thermal-tactile stimulation, and expiratory muscle strength training (EMST)<sup>[6]</sup>.

The present study aimed at evaluating the effects of treatment for dysphagia in Parkinson's disease, accordingly the present systematic review incorporates all therapies available for oropharyngeal dysphagia in Parkinson's disease, including an update on rehabilitative therapies. The different types of therapy are grouped into four main therapy groups: rehabilitative, surgical, pharmacologic, and other.

## MATERIALS AND METHODS

### Data Sources

We carried out a systematic review of RCTs, prospective and retrospective studies of operated from January 1960 to July 2017. This review was performed according to the PRISMA guidelines [7]. Literature searches of Pubmed, Embase, CENTRAL and SCOPUS Cochrane Library between January 1960 until July 2017 were performed. The search terms were used in combinations and together with the Boolean operators OR and AND; Search terms used were: “Dysphagia Therapy”, “Parkinson’s Disease”, “oropharyngeal dysphagia”.

Data extraction was performed by two independent reviewers and consisted of analysis of critical appraisal criteria per included study. Very few differences in rating were settled by consensus agreement after a discussion. If consensus could not be reached, a third review author was consulted for adjudication. The critical appraisal criteria were rated as ‘yes’, ‘no’ or as ‘unknown’ when insufficient information was provided and are summarized in **Fig. 1**.

The present quality assessment tool, like many other validated ones, does not incorporate a quality score [8]. Finally, a meta-analysis was not carried out as most of the studies were not of sufficient quality to warrant doing so.

### Study Selection and Criteria

Search results were screened by scanning abstracts for the following

### Inclusion criteria

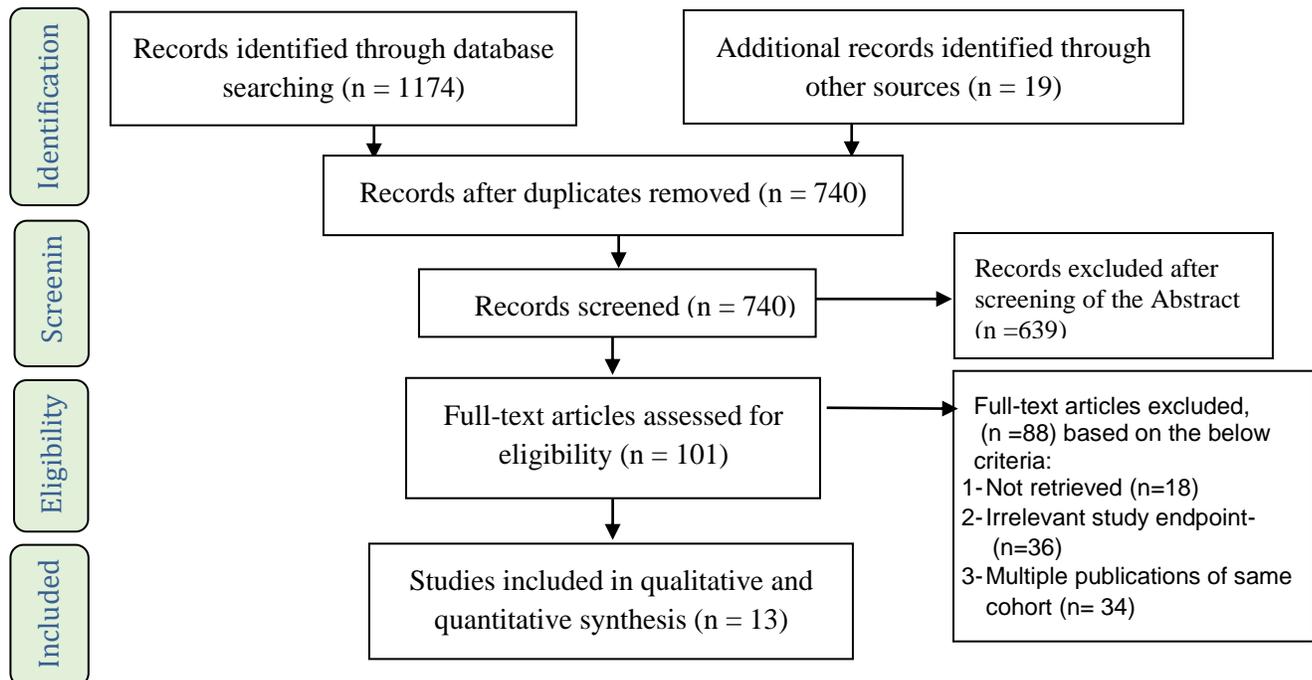
- Publications in English, German, French or Spanish language articles
- Publications with pre- and post-intervention data N =10
- Participants Patients diagnosed with Parkinson’s disease
- Patients with or without swallowing disorders
- Patients without Deep Brain Stimulation (DBS) Adults

### Exclusion criteria

- *In -vitro* laboratory studies in experimental set-up
  - Studies involving experiments on animals
  - Studies including patients with DBS since dysphagia has often been described as a side-effect of DBS
- The study was done after approval of ethical board of King Abdulaziz university.

## RESULTS

Electronic database search identified 1174 publications in addition to another 19 publications that were found through manual research. After removal of duplicates, abstracts and titles, 101 publications were assessed as identified from title and abstract, and 639 papers were excluded. 18 papers full text could not be retrieved and another 34 papers with the same cohort. There were also 36 papers excluded because they did not assess the Impact of Dysphagia Therapy in Parkinson’s. We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines in reporting the results (**Figure 1**).



**Figure 1: PRISMA flow diagram showing the selection criteria of assessed the studies<sup>22</sup>.**

Number of patients, disease severity based on the Hoehn and Yahr scale (H-Y scale)<sup>[9]</sup>, the kind of therapy used, evaluation techniques, outcome parameters, blinded rater(s), on/off-motor phase, and the authors' key findings were summarized in Table 1 and Table 2. The fluctuation in daily performance of Parkinson patients on long-term L-dopa therapy is known as the "on/off" phenomenon<sup>[10]</sup>. The number of subjects refers to the group of subjects on which the study results were based, i.e., dropouts were excluded. All studies were described briefly.

**Table 1: Study characteristics and design**

Author	Publication Year	Study type	Treatment(s) groups	Data analysis	Subjects Hoehn & Yahr scale (H-Y)
<b>Rehabilitative treatment(s)</b>					
El Sharkawi <i>et al.</i> <sup>[11]</sup>	2002	Non-RCT	Lee Silverman Voice Treatment (LSVT)	Statistical analysis (analysis of variance)	<i>N</i> = 8 H-Y: II-IV
Nagaya <i>et al.</i> <sup>[12]</sup>	2000	Non-RCT	1. Five exercises: range of tongue motion exercises, resistance exercises, exercises to increase the adduction of vocal folds, Mendelsohn maneuver range of motion exercises in the neck, trunk, and shoulder joints.	Statistical analysis (Wilcoxon signed rank test)	<i>N</i> = 10 H-Y: III ( <i>N</i> = 8) and IV ( <i>N</i> = 2)
Pinnington <i>et al.</i> <sup>[13]</sup>	2000	Non-RCT	Verbal cueing while presenting a spoon to the mouth	Statistical analysis (paired <i>t</i> test)	<i>N</i> = 12 H-Y: II-V
Troche <i>et al.</i> <sup>[14]</sup>	2008	Non-RCT	Bolus modification (thin liquid and pudding-thick boluses): single session	Statistical analysis (analysis of variance, Kruskal-Wallis)	<i>N</i> = 10 H-Y: II-III
Logemann <i>et al.</i> <sup>[15]</sup>	2008	Non-RCT	Bolus modification (honey-thick, nectar-thick), postural changes (chin down): single session	Descriptive statistics	<i>N</i> = 228 PD H-Y: I-V
<b>Surgical treatment(s)</b>					
Born <i>et al.</i> <sup>[16]</sup>	1996	consensus or expert opinion	Cricopharyngealmyotomy (Zenker's diverticulectomy)		<i>N</i> = 4
Byrne <i>et al.</i> <sup>[17]</sup>	1994	consensus or expert opinion	Cricopharyngealmyotomy (Zenker's diverticulectomy)		<i>N</i> = 3 H-Y: II-IV
<b>Pharmacologic treatment(s)</b>					
Iwasaki <i>et al.</i> <sup>[18]</sup>	2000	Non-RCT	G1: "Banxia Houpo Tang" (BHT) 3 × 1.5 g/day for 4 weeks, 30 min before each meal ( <i>N</i> = 22 PD) G2: lactate 3 × 1.5 g ( <i>N</i> = 6 PD)	Statistical analysis (paired <i>t</i> test)	<i>N</i> = 28 H-Y: mean 2.8-3
Lim <i>et al.</i> <sup>[19]</sup>	2008	Non-RCT	After withholding antiparkinsonian medication for at least 12 h, the usual dose of levodopa is administered.	Statistical analysis (paired <i>t</i> test, McNemar tests)	<i>N</i> = 10 H-Y: I-IV

Bushmann <i>et al.</i> <sup>[20]</sup>	1989	Non-RCT	G1: Levodopa: intake of a subject's usual dose of levodopa after withholding antiparkinsonian medications overnight. (> 8 h) (N = 15) G2: Therapeutic maneuvers (N = 3)	Descriptive statistics	N = 15 H-Y: I-IV
Fuh <i>et al.</i> <sup>[21]</sup>	1997	Non-RCT	200 mg levodopa (in combination with 50 mg benserazide) orally	Descriptive statistics	N = 12–15? H-Y: mean 1.9
<b>Other treatment(s)</b>					
Heckmann <i>et al.</i> <sup>[22]</sup>	2000	Non-RCT	Mandibular implant overdentures	Descriptive statistics	N = 3 H-Y: III
Restivo <i>et al.</i> <sup>[23]</sup>	2002	consensus or expert opinion	Percutaneous injection of botulinum neurotoxin type A in the cricopharyngeal muscle		N = 4

**Table 2:** techniques outcome and author's conclusion

Author	Publication Year	Evaluation techniques Outcome parameters [ON/OFF motor phase]	Author(s)' conclusions
<b>Rehabilitative treatment(s)</b>			
El sharkawi <i>et al.</i> <sup>[11]</sup>	2002	Video fluoroscopy of swallowing	The incidence of the swallow motility disorders is consistently reduced after LSVT and some timed variables of swallowing improve significantly. Findings suggest that LSVT may activate neuromuscular control of the entire aerodigestive tract, improving function in both the oral tongue and the tongue base during the oral and pharyngeal stages of swallowing.
		Outcome parameters:	
		• Identification of physiologic oropharyngeal motility disorders	
		• Timed variables of swallowing	
		• Oropharyngeal swallow efficiency	
Nagaya <i>et al.</i> <sup>[12]</sup>	2000	Blinded judgment	[the same time of day and medicine cycle for each patient]
		Electromyography (EMG)	
		Outcome parameter:	
Pinnington <i>et al.</i> <sup>[13]</sup>	2000	• Premotor time (PMT)	[ON motor phase]
		Exeter Dysphagia Assessment Technique (EDAT): nasal airflow, contact of the lips/tongue with a spoon, recording of sounds associated with swallowing.	
		Outcome parameters:	
		• Direction of respiration immediately preceding and following each swallow	
		• Number of swallows	
		• Duration of the "oral part"	
			Verbal cueing results in a significant reduction in the duration of the oral part but has no impact on the duration of the pharyngeal part of or the mean number of swallows. The use of the verbal cue improves the oral and lingual bradykinesia.

		<ul style="list-style-type: none"> <li>• Duration of the “pharyngeal part”[ON motor phase]</li> </ul>	
Troche <i>et al.</i> <sup>[14]</sup>	2008	Videofluoroscopy of swallowing	Analysis reveals significant differences between oral transit time, number of tongue pumps, and P-A scale with respect to bolus consistency. Oral transit time and the number of tongue pumps increase with thicker boluses, P-A score is higher for thinner boluses. No significant differences are found for pharyngeal transit time.
		Outcome parameters:	
		<ul style="list-style-type: none"> <li>• Timed variables of swallowing</li> <li>• Qualitative variables of swallowing (P-A scaleh, tongue pumps).</li> </ul>	
		Blinded to patients’ identity[ON motor phase]	
Logemann <i>et al.</i> <sup>[15]</sup>		<ul style="list-style-type: none"> <li>• Videofluoroscopy of swallowing</li> </ul>	39% of all participants aspirate on all three interventions. 12% aspirate on two of the three interventions. 17% aspirate on one of the three interventions. 32% aspirate on none of the three interventions.
		Outcome parameter:	
		Qualitative variable of swallowing (aspiration)	
<b>ical treatment(s)</b>			
Born <i>et al.</i> <sup>[16]</sup>		Videosophagographya	All four patients have experienced excellent and sustained relief of esophageal symptoms following surgery, providing further support for the primacy of cricopharyngeal dysfunction in causing dysphagia in these patients. The patients tolerate myotomy extremely well and none developed aspiration.
		Esophageal manometrya	
Byrne <i>et al.</i> <sup>[17]</sup>		Videosophagographya	Three patients with cricopharyngeal dysfunction have undergone cricopharyngealmyotomy with excellent results.
		Esophageal manometrya	
<b>Pharmacologic treatment(s)</b>			
Iwasaki <i>et al.</i> <sup>[18]</sup>	2000	Submental EMG	Despite all patients having long-term levodopa therapy, the traditional Chinese medicine improves the swallowing reflex in the Parkinson patients significantly. Mechanisms of this improvement are unknown.
		Outcome parameter:	
		<ul style="list-style-type: none"> <li>• Timed variables of swallowing (latency time of the swallowing reflex = timing from the injection of the bolus to the onset of swallowing)</li> </ul>	
		Blinded to therapy	
Lim <i>et al.</i> <sup>[19]</sup>	2008	SWAL-QOLa	Swallowing efficiency may be reduced with levodopa medication. No association is found between levodopa and coordination of swallowing and respiration, laryngeal penetration, or tracheal aspiration, indicating that the risk of aspiration may remain unchanged. It is speculated that levodopa therapy might actually reduce swallowing efficiency while keeping the risk of aspiration unchanged in patients with PD.
		EMG with nasal cannula	
		FEES	
		Outcome parameters:	
		<ul style="list-style-type: none"> <li>• Coordination of swallow and respiration</li> <li>• Timed variables of swallowing</li> </ul>	
		<ul style="list-style-type: none"> <li>• Qualitative variables of swallowing (visuoperceptual)</li> </ul>	
Bushmann <i>et al.</i> <sup>[20]</sup>	1989	MBS	G1: 5/15 patients with abnormal swallows show improvement in swallowing following an oral dose of levodopa. The degree of improvement ranges from mild to dramatic. Transit
		Outcome parameters:	
		<ul style="list-style-type: none"> <li>• Swallowing behaviors (mastication, bolus formation, oral stasis, lingual peristalsis, tongue</li> </ul>	

		movements, etc.)	times for thick boluses show the greatest improvement. Higher doses of levodopa do not provide additional benefit. G2: The voluntary airway protection technique eliminates aspiration in 2/3 patients.
		[Pretreatment MBS off]	
		[Posttreatment MBS on]	
Fuh <i>et al.</i> [21]	1997	MBS	More than half of the patients experience improved swallowing function after levodopa treatment due to a reduction of bradykinesia and rigidity of the tongue. Aspiration is found in 3 patients. Two of these 3 patients reveal no post-levodopa aspiration. The dopaminergic mechanism may play a role in oropharyngeal control of swallowing.
		Outcome parameters:	
		• Timed variables of swallowing	
		• Qualitative variables of swallowing	
		[Pretreatment MBS off]	
		[Posttreatment MBS on]	
<b>Other treatment(s)</b>			
Heckmann <i>et al.</i> [22]	2000	Modified symptom questionnaire on gastrointestinal (GI) symptoms by Horowitz <i>et al.</i> (4-point scale: 0 = none, 3 = severe complaints).	On the gastrointestinal scale, all patients have improved from a mean score of 8.7 to 5.7 despite a general deterioration of the PD scores during follow-up. The implant-prosthetic treatment increases chewing ability and appears to enhance oropharyngeal predigestion.
		Body weight (kg)	
		Self-rating scale for chewing abilities	
Restivo <i>et al.</i> [23]	2002	Clinical examination	Given its safety and effectiveness, the authors propose that treatment with botulinum neurotoxin type A may be a successful alternative to invasive procedures or may be a useful tool for identifying patients who might benefit from surgical myotomy.
		Videofluoroscopy of swallowing (visuoperceptual rating?)	
		Electromyography	

## DISCUSSION

In the present systematic literature review, the methodological quality of the included studies (Fig. 1) has improved compared to the previous studies.

### 1. Rehabilitative Treatment

El Sharkawi *et al.* [11] studied the effects of 1 month of Lee Silverman Voice Treatment (LSVT) on swallowing and voice in eight patients with idiopathic Parkinson's disease and dysphagia. After 1 month of LSVT, the authors concluded that LSVT seemed to be effective in improving neuromuscular control of the entire upper aerodigestive tract, improving oral tongue and tongue base function during the oral and pharyngeal phases of swallowing.

Troche *et al.* [14] evaluated the effect of bolus consistency on timing and safety of swallowing in patients with Parkinson's disease. Oral transit time and the number of tongue pumps increased with thicker boluses and the P-A score was higher for thinner boluses. No significant differences were found for pharyngeal transit time.

Logemann *et al.* [15] performed a study to identify which of the three treatments for aspiration on thin liquids (chin-down posture, nectar-thickened liquids, or honey-thickened liquids) resulted in the most successful immediate elimination of aspiration during a video-fluoroscopic swallow study in patients with dementia and/or Parkinson's disease. 228 Parkinson patients underwent all three interventions in randomly assigned order. 39% of participants with Parkinson's disease without dementia aspirated on all three interventions. 12% aspirated on two of the three interventions. 17% aspirated on one of the 3 interventions. 32% aspirated on none of the three interventions. Based on these descriptive results the authors concluded that the most frequently successful intervention to eliminate thin-liquid aspiration immediately was the honey-thickened liquid, followed closely by the nectar-thickened liquid and then the chin-down posture.

### 2. Surgical Treatment

Two articles provided anecdotal data about surgical treatment for dysphagia in Parkinson's

disease. In the articles issued by Born et al.<sup>[16]</sup> and Byrne et al.<sup>[17]</sup> cricopharyngeal sphincterotomy was performed in very small groups of patients.

Born et al.<sup>[16]</sup> described four patients who experienced excellent and sustained relief of esophageal symptoms following surgery, providing further support for the primacy of cricopharyngeal dysfunction in causing dysphagia in these patients. The patients tolerated myotomy extremely well and none developed aspiration. Byrne et al.<sup>[17]</sup> studied three patients with cricopharyngeal dysfunction who had undergone cricopharyngeal myotomy with excellent results. Only pretreatment measurements consisting of manometry and videoesophagography were performed in both studies. No posttreatment measurements were described, although the authors' own conclusions were included.

### 3. Pharmacologic Treatment

The study carried by Iwasaki et al.<sup>[18]</sup> described the positive therapy effects of traditional Chinese medicine "BanxiaHoupo Tang" (BHT) in improving the swallowing reflex of patients with Parkinson's disease. After therapy a statistically significant decrease of swallowing reflex time was demonstrated in the patient group receiving BHT. It remains unclear which components in the extract of dried plants were responsible for the improvement of the swallowing function.

Bushmann et al.<sup>[20]</sup> evaluated the effects of the intake of the usual dose of levodopa were evaluated by means of pre- and posttreatment MBS in 20 patients with Parkinson's disease. The voluntary airway protection technique eliminated aspiration in two of three patients. According to the authors, higher doses of levodopa did not provide additional benefit.

Fuh et al.<sup>[21]</sup> examined the oropharyngeal swallowing ability in 19 Parkinson's disease patients using MBS before and after administering oral levodopa (200 mg) in combination with benserazide (50 mg). Based on descriptive statistics, the authors concluded that more than half of the patients experienced improved swallowing function after levodopa treatment due to a reduction of bradykinesia and rigidity of the tongue.

### 4. Other Treatments

Heckmann et al.<sup>[22]</sup> studied the benefit of using dental implants combined with overdentures to improve chewing and pre-ingestion capacity in three severely handicapped Parkinson patients. The authors interpreted improved chewing capacity, a

moderate gain in body weight, and an improved GI score as signs of improved predigestion.

In the study carried by Restivo et al.<sup>[23]</sup> the effect of percutaneous injected botulinum toxin for cricopharyngeal dysfunction was evaluated in four patients with Parkinson's disease by means of video fluoroscopy of swallowing and electromyography. The authors concluded that given its safety and effectiveness, the treatment with botulinum neurotoxin type A may be a successful alternative to invasive procedures or may be a useful tool for identifying patients who might benefit from surgical myotomy.

### CONCLUSION

Few reports have been published on the effect of therapies for oropharyngeal dysphagia in PD. For dopaminergic treatment, consensus has yet to be reached whether it affects swallowing physiology or not. In case of persistent dysphagic symptoms despite pharmacological treatment, alternative approaches such as logopedic dysphagia treatment can be considered. Subsequently, several rehabilitative therapies, including EMST, and VAST, have been successful. Much work still needs to be done to improve the management of oropharyngeal dysphagia in patients with PD. Further research should focus on several remaining gaps in our knowledge on treatment interventions for oropharyngeal dysphagia in PD. Well-designed RCTs using larger scale of populations are essential to evaluate clinical applicability and the potential therapeutic effects of new treatment techniques.

The therapy effects of more recently developed other treatment methods such as implant-prosthetic treatment and percutaneous injection of botulinum neurotoxin type A in the cricopharyngeal muscle on dysphagia is rather promising. Nevertheless, in this field too large well-designed trials are required.

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