Original Investigation | Özgün Araştırma

Gazi Med J 2025;36(3):300-306

DOI: http://dx.doi.org/10.12996/gmj.2025.4395

Do We Cause Dysphagia When Treating Spasmodic Dysphonia with Botox?

Spasmodik Disfoni'yi Botoksla Tedavi Ederken Disfajiye Neden Oluyor muyuz?

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ABSTRACT

Objective: Spasmodic dysphonia (SD) is a neurological movement disorder involving the laryngeal muscles. There are three main types: adductor, abductor, and mixed type. Adductor type is the most common and mixed type is the rarest. Botox, the gold standard in treatment, is applied to the affected muscle group according to the type of SD. Dysphagia often occurs as a side effect of botulinum toxin injection treatment in spasmodic dystonia. Dysphagia may sometimes be seen secondary to SD.

Methods: This study included 8 patients with adductor SD without dysphagia and 8 healthy subjects. The total number is 16. Swallowing evaluation of both groups was performed by fiberoptic endosopic evaluation of swallowing (FEES), electromyography (EMG) and ultrasound (US).

Results: Swallowing functions of patients with adductor SD were reevaluated after botox injection into the thyroarytenoid muscle. No significant difference was observed in both groups .

Conclusion: In our study, our patient group consisted of patients with SD without dysphagia, and dysphagia was not observed in patients evaluated with FEES, EMG and US after Botox.

Keywords: Swallowing/dysphagia, voice/dysphonia, laryngeal dystonia/tremor

ÖZ

Amaç: Spazmodik disfoni (SD) laringeal kasları içeren nörolojik bir hareket bozukluğudur. Üç ana tipi vardır: addüktör, abdüktör ve mikst tip. Addüktör tip en sık görülen, mikst tip ise en nadir görülen tiptir. Tedavide altın standart olan botoks, SD tipine göre etkilenen kas grubuna uygulanır. Spazmodik distonide yutma güçlüğü sıklıkla botulinum toksin enjeksiyon tedavisinin bir yan etkisi olarak ortaya çıkar. Disfaji bazen SD sekonder olarak da görülebilir.

Yöntemler: Bu çalışmaya disfajisi olmayan adduktor SD olan 8 hasta ve 8 sağlıklı birey dahil edildi. Toplam sayı 16'dır. Her iki grubun yutma değerlendirmesi fiberoptik endosopik yutma değerlendirmesi (FEES), elektromiyografi (EMG) ve ultrasonografi (USG) ile yapıldı.

Bulgular: Addüktör SD'li hastaların yutma fonksiyonları tiroaritenoid kasa botoks enjeksiyonundan sonra tekrar değerlendirildi. Her iki grupta da anlamlı bir fark gözlenmedi

Sonuç: Çalışmamızda hasta grubumuz disfajisi olmayan SD'li hastalardan oluşmakta olup, Botoks sonrası FEES, EMG ve USG ile değerlendirilen hastalarda disfaji gözlenmemiştir

Anahtar Sözcükler: Yutma/disfaji, ses/disfoni, laringeal distoni/tremor

Cite this article as: Altan E; Barmak E, Karaca Umay E, Çadallı Tatar E. Do we cause dysphagia when treating spasmodic dysphonia with botox? Gazi Med J. 2025;36(3):300-306

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Received/Geliş Tarihi: 11.2.2025
Accepted/Kabul Tarihi: 12.3.2025
Publication Date/Yayınlanma Tarihi: 11.07.2025

INTRODUCTION

Spasmodic dysphonia (SD) or laryngeal dystonia is a neurologic disorder characterized by involuntary intermittent contraction of intrinsic laryngeal muscles (1,2). According to the muscles involved, there are three forms of SD: the adductor, the abductor, and the mixed form. Adductor SD (ADSD) is characterized by an effortful and strained voice as if choking by contracting the muscles that provide adduction and blocking the airflow In ADSD, the cords do not close during phonation due to abductor paralysis, which is associated with dyspnea and aphonia (3,4). ADSD is the most common type in the clinic; mixed type is less common and it is difficult to diagnose (5).

The treatment of SD involves botulinum toxin (BT) injection into the thyroarytenoid muscle for the adductor type and the posterior cricoarytenoid muscle for the abductor type. This procedure is sometimes performed under electromyography (EMG) guidance. In some cases, surgical procedures and voice therapy may also be considered. Botox injection is the gold standard. Botox prevents muscle contractions by binding to acetylcholine receptors at the neuromuscular junction and inhibiting the release of acetylcholine. Surgical techniques include type 2 thyroplasty (6,7), myectomy (thyroarytenoid muscle) (8) and selective laryngeal denervation-reinnervation (9). These surgical procedures are used to treat for adductor type of SDVoice therapy is a part of the treatment, but its effectiveness is limited. It can be used in combination with other treatments.

Swallowing has some phases; it is a complex behavior that takes place with the work of oral, pharyngeal, and esophageal muscles (10,11). Dysphagia can be defined as the difficulty in the process that starts with chewing in the mouth and continues as food moves to the stomach. Oral dysphagia can be defined as any difficulty in the preparation of a bolus. Pharyngeal dysphagia may be caused by absence or delay of the swallowing reflex, and esophageal dysphagia may be caused by esophageal or sphincter disorder (10,12).

Dysphagia may also occur as a result of Botox injections administered for the treatment of spasmodic dystonia. One of the most common side effects after botox injection in cervical dystonias and spasmodic dysphonias is defined with an incidence rate ranging from 10% to 90% (13-15). The use of ultrasound (US) and EMG during injections can help reduce these side effects (14). Very few studies have evaluated swallowing before and after treatment (16-18). However, many studies have not focused extensively on dysphagia secondary to botox (19-21). The involuntary pharyngeal phase of swallowing is particularly affected, and premature leaking is observed with fluids. This condition, which can be treated with diet modifications, is often overlooked because of its transient nature.

No study has objectively and multimodally evaluated the effect of BT in on swallowing function in these patients. Therefore, we aimed to evaluate the swallowing functions in patients with spasmodic dystonia without dysphagia symptoms and to investigate the effect of BT treatment on the swallowing function.

MATERIAL AND METHODS

The University of Health Sciences Türkiye, Ankara Etlik City Hospital No. 1 Clinical Research Ethics Committee (decision number: AEŞH-EK1-2023-597, date: 04.10.2023) approved before the research began. We obtained informed consent from all participants.

Assessment Tools

First, demographic and disease characteristics were obtained from all participants. Then, fiberoptic endoscopic evaluation swallowing (FEES) electrophysiology, and ultrasonographic (USG) evaluation were performed to evaluate swallowing functions.

Demographic and disease characteristics: patients and volunteers, including age, gender and educational status, as well as dystonia duration of patients were recorded.

Swallowing evaluation: the following three assessment methods were used to evaluate the swallowing functions of the participants.

a) Fiberoptic Endoscopic Evaluation

b) Swallowing Electrophysiology

c) Ultrasonographic Evaluation

Flexible Fiberoptic Endoscopic Evaluation of Swallowing (FEES)

The most important and gold standard diagnostic methods for the diagnosis of dysphagia (OD) are FEES and videofluoroscopic swallowing study (VFSS) (22). The advantages of FEES are that it can be performed in any environment, including the patient's bedside; it has no radiation effect. Its disadvantages are that the passage cannot be seen clearly when the pharynx is closed during swallowing (22). Endoscopic evaluation of the patients was performed by the same specialist, with the patient in a sitting position, using a 3.4 mm diameter channelless fiberoptic nasopharyngoscope, light source, camera, monitor, and DVD recorder (Karl Storz GmbH & Co KG, Tuttlingen, Germany). Local anesthetics were not used during this test. Aspiration or penetration of water up to 100 milliliters was used to determine the residue. Yogurt was used as a semi-solid and biscuits were used as a solid. The findings were recorded and examined according to the Dzeiwas endoscopic evaluation protocol, to score the dysphagia levels of our patients between 1 and 6. Score 1 was considered “normal swallowing function”, while scores between 2 and 6 were considered “dysphagia” and were graded from minimal to severe (23).

Swallowing Electrophysiology

The physical medicine and rehabilitation specialist performed the electrophysiological evaluation with a 10-channel EMG device by Medelec Synergy (Oxford, England) (24,25). The motor components and muscles involved in swallowing are evaluated with sEMG. In particular, sEMG provides the amplitude, peak, and latency of muscle contraction, and magnitude and temporal parameters such as duration and frequency (26,27). During swallowing, the shMs between the mandible and the hyoid provide hyoid elevation, and these muscles have important roles in the pharyngeal phase of swallowing (26,28). The patients were asked to sit with their heads in a neutral position. An active disk electrode was placed on the submental muscles, a reference disk electrode was placed on the chin, and a laryngeal (piezoelectric) sensor was placed in the coniotomy area and fixed in place. The signals were recorded with a channel, filtered with a band-pass of 0.01-20 Hz. The first of the two deviations obtained with the piezoelectric sensor indicated the elevation of the larynx, and the second indicated the end of the pharyngeal reflex phase. The beginning of the first deviation is called “0”, while the beginning of the second deviation that indicates

the end of the pharyngeal reflex is called "2". The 0-2 interval is the time elapsed during the elevation and floating of the larynx. In other words, the 0-2 interval is the time that triggers the swallowing reflex. The time between the point (A) that is the beginning of the SM-EMG and the first point (0) that the swallowing reflex begins. The "A-0" time interval is the time between the voluntary contraction of the submental muscle complex and the triggering of the swallowing reflex, which provides the duration of the oral phase. The A-C time interval is recorded as the total oropharyngeal swallowing time , representing the period during which SM muscle activity is present.

Ultrasonographic (USG) Evaluation

USG is also used in the evaluation of swallowing (29). The evaluation includes grading the cross-sectional area (CSAs), thickness, contractility, and echogenicity of the muscle (30). The oral and shMs can be easily identified using USG, and these measurements can also be made during muscle movement, thus they can be used to evaluate muscle function (31).

All measurements were performed in the supine position. Real-time imaging and CSAs (geniohyoid and bilateral anterior digastric muscles) were acquired with an USG device (GE Logiq P5, General Electric, Korea) and a 7-12 MHz linear array transducer. The geniohyoid and anterior digastric muscles were measured while the patients were in a relaxed position with their tongue in the mouth. The distance between the mandible bone and the hyoid bone was measured, and the skin was marked one-third of the way behind the inferior border of the mandible. The transducer was placed in the coronal plane to measure the CSAs of the muscles.

Study Protocol

All subjects were assessed for swallowing. The pre-treatment results in the patient group and the healthy group were compared. Evaluation of parameters for patients was performed at 1 month after botulinum toxin administration. The impairment levels for the patient group were compared pre- and post-treatment.

Participants

A total of 16 subjects were included in the study, consisting of 8 patients with SDbut without dysphagia symptoms who were planned to undergo botulinum toxin injection into their thyroaritenoid muscles, and 8 healthy volunteers who were age- and gendermatched to these patients.

Subjects who had any metabolic/endocrine and progressive central or peripheral nervous system diseases, had a past surgical history, or were using drugs that can cause swallowing dysfunction were excluded from the study. In addition, patients with multifocal or segmental dystonia who described difficulty swallowing were also excluded from the study.

Botulinum Toxin Injection

In SD, involuntary closure of the vocal cords causes speech difficulties. The gold standard treatment for these patients is periodic injections of botulinum toxin A (BTX-A) into these muscles to prevent them from contracting involuntarily. In the adductor type, the improvement in voice after Botox is 8.0 to 15.1 weeks (32,34). Commonly reported side effects of BTX-A injections include a slightly breathy voice (25-35% of patients) and cough or dysphagia (especially with liquids), affecting 10% of patients. The dose and timing of the patient's next injection are determined by the patient's side effects (35).

In our study patients with adductor type SD were injected with 2.5 units of onabotulinum toxin Type A (Botox®) botulinum toxin into both thyroarytenoid muscles with EMG guidance. After treatment, patients' satisfaction was assessed using a Likert scale with options: "I am satisfied", "I am not satisfied", and "I am neither satisfied nor dissatisfied".

Statistical Analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences, version 20.0 for Windows (SPSS Inc., Chicago, IL, USA). Normality of the continuous variables was assessed by the Kolmogorov-Smirnov test. Descriptive statistics were shown as mean (SD: standard deviation) for continuous variables and frequencies (%) for nominal variables. Statistically significant differences in repeated measurements within the groups were evaluated with the Wilcoxon-Friedman tests. The Mann-Whitney U test was used for the significant differences between groups. The results were considered significant for $p<0.05$.

RESULTS

While 5 of the 16 (31.3%) patients were female, 11 (68.7 %)were male and the mean age was 45.12±7.28 years of study subjects (n=16). Distribution and comparison of demographic characteristics of subjects, according to the groups, are presented in Table 1.

The disease duration of the patients was 2.74 (SD=1.26) years. None of the subjects had dysphagia according to fiberoptic endoscopic evaluation. Comparison of electrophysiological and USG pre- and post-treatment evaluation results of groups is shown in Table 2 and Table 3.

Electrophysiologically, while the swallowing triggering reflex times (0-2) and total swallow durations (A-C) of patients were longer than those of healthy individuals ($p<0.05$), the oral phase time was similar ($p>0.05$). Moreover, the geniohyoid muscle area was larger than that of the healthy group ($p=0.023$).

It was seen that the swallowing triggering reflex time and total swallow durations of patients were similar to that of healthy individuals during the first month of follow-up after Botulinum toxin

Table 1. Demographic characteristics of subjects according to groups

	Patient group	Healthy group	p
Age (years) mean (SD)	47.26 (7.19)	42.60±8.94	0.187
Gender n (%)			
Male	6 (75)	5 (63.5)	0.271
Female	2 (25)	3 (37.5)	
Educational status n (%)			
5 years	1 (12.5)	0	
8 years	1 (12.5)	3 (37.5)	
11 years	2 (25)	1 (12.5)	0.094
More than 11 years	4 (50)	4 (50)	

SD: Standard deviation

Table 2. Electrophysiological and ultrasonographic pre-treatment evaluation results of subjects

	Patient group mean (SD)	Healthy group mean (SD)	p
Swallowing intervals (msn)			
0-2 interval	525.20 (96.23)	317.28 (86.22)	**0.011**
A-0 interval	175.01 (76.31)	168.14 (44.71)	0.537
A-C interval	681.52 (104.14)	487.43 (113.65)	**0.007**
Anterior digastric (cm^2)			
Right	0.99 (0.34)	0.97 (0.25)	0.762
Left	0.97 (0.41)	0.91 (0.89)	0.613
Geniohyoid (cm^2)	1.97 (0.85)	1.42 (0.21)	**0.023**

SD: Standard deviation

Table 3. Electrophysiological and ultrasonographic post-treatment evaluation results of subjects

	Patient group (post-treament) mean (SD)	Healthy group mean (SD)	p
Swallowing intervals (msn)			
0-2 interval	401.14 (87.62)	317.28 (86.22)	0.078
A-0 interval	173.15 (64.98)	168.14 (44.71)	0.619
A-C interval	513.87 (79.33)	487.43 (113.65)	0.092
Anterior digastric (cm^2)			
Right	0.98 (0.47)	0.97 (0.25)	0.915
Left	0.96 (0.72)	0.91 (0.89)	0.261
Geniohyoid (cm^2)	1.95 (0.23)	1.42 (0.21)	**0.028**

SD: Standard deviation

application. After treatment, all patients were satisfied (n=8, 100%). Moreover, 5 patients (62.5%) said that it was easier to eat solid foods than before. Also, none of the patients had aspiration findings.

DISCUSSION

Botox injection in SD was first performed by Blitzer et al. (36) in 1984. Dysphagia may be observed after BTX injection, and its frequency is between 10-90% (15,37,38), and this side effect can be reduced by performing BTX injection with EMG and USG guidance (38). In some studies, no signs of dysphagia were detected when the swallowing evaluation was compared before and after treatment (16,17,18). Alterations in swallowing, such as the presence of food in the epiglottic vallecula due to delayed swallowing reflex, have been described as changes in the pharyngeal phase of swallowing in these patients before treatment (39-41). In our study, this was not detected in the swallowing evaluation, and patients without dysphagia were included to show whether Botox has side effects.

In the literature, dysphagia can be seen in patients with cervical dystonia before and after Botox treatment or surgery. This dysphagia has been explained by two different mechanisms. One of these mechanisms is the abnormal position of the neck, which causes anatomical asymmetry in swallowing, in cervical dystonia (42-45). However, this interpretation does not explain dysphagia in spasmodic dystonias without abnormal neck movements and in some oromandibular dystonias. The second possibility is neurogenic dysfunction, which causes delayed swallowing and other oropharyngeal findings (42-45). Since our patient group consists of patients with adductor type spasmodic dysphonia, there is no anatomical asymmetry.

FEES described by Langmore et al. (46) is the gold standard for swallowing evaluation. FEES and videofluoroscopic swallowing evaluation are crucial methods used in the diagnosis of oropharyngeal dysphagia (OD) (22). FEES has many advantages, including no radiation exposure, portability, applicability to neurological patients with limited mobility at the bedside, and visual monitoring of swallowing, salivation, and residual food transit. Although FEES was initially developed by a speech and language pathologist, it is very commonly performed by healthcare professionals (22,23,46). In the present study, all patients were evaluated with FEES before and after Botox injection, and no signs of dysphagia were detected in any evaluation' or 'In the present study, all patients were evaluated with FEES before and after Botox injection. No signs of dysphagia were detected in any evaluation. However, a multidisciplinary approach is essential for the evaluation of dysphagia, including not only FEES but, also videofluoroscopic swallowing evaluation, EMG, and USG.

Some studies have examined the utility of surface EMG (sEMG) of the submental muscles in swallowing rehabilitation. In particular, sEMG has been used to assess swallowing and to examine hyolaryngeal elevation, pre- and post-swallow muscle contraction, and its duration (47-50). sEMG is a valid and reliable method for assessing normal swallowing (51). sEMG is a non-invasive tool for assessing specific aspects of the complex muscle activity involved in swallowing. sEMG is simple and reliable to perform (52,53). There are SEMG studies in the literature on neck muscle activity during squeezing or chewing in patients with normal swallowing and temporomandibular disorders. However, fewer studies have examined the SEMG behavior of neck muscles during swallowing (54-58). It records electrical activity from the anterior digastric muscle and suprahyoid area muscles (i.e., geniohyoid and mylohyoid) (54). The most important things for swallowing are sEMG findings showing hyoid elevation in the anterior compartment and contraction of the submental muscles (49). In the literature, swallowing time varies between 0.80 and 1.60 seconds (55,56). This time does not change from age 12 to age 70. After the age of 70, swallowing time increases significantly (51,52,57,58). In the study by C. Ertekin et al. (17) prolonged SM muscle complex activity during swallowing (68%) was observed. Prolonged laryngeal displacement was observed in 42% of patients with cervical dystonia, while decreased SM muscle activity was observed in 31%. These two findings are also seen in Parkinson's disease (17).

In the present study, before Botox, the patients' swallowing reflex time (0-2) and total swallowing time (A-C) were significantly longer than those of healthy individuals ($p<0.05$), while oral phase times were similar ($p>0.05$).' or 'In the present study, the swallowing reflex duration (0-2) and total swallowing time (A-C) of patients before Botox were significantly longer than those of healthy individuals ($p<0.05$), and the oral phase durations were similar ($p>0.05$).

In the first month after botulinum toxin injection, it was seen that, patients' swallowing reflex time and total swallowing time were similar to healthy individuals. All patients were satisfied after treatment (n=8, 100%). In addition, 5 patients (62.5%) said that eating solid foods was easier than before. Moreover, none of the patients had any signs of aspiration. In this study, the selection of patients with SD affects the results.

Coordinated contraction of the suprahyoid muscle (shM) complex, which includes the digastric, mylohyoid, and geniohyoid muscles, causes displacement of the hyoid bone and promotes bolus propulsion into the esophagus. Most studies have evaluated the thickness, CSAs, and echo density of the tongue or other swallowing muscles (digastric, geniohyoid, and mylohyoid) when evaluating dysphagia with USG (59-62). During swallowing, the shM contracts and a change in thickness and upward movement occur. The severity of dysphagia depends on the difference in the displacement of these muscles which play an important role in the pharyngeal phase of swallowing (63-65). In some studies, the shM complex and displacement of stroke, ALS, MG (64-70), and inflammatory myopathy, whose dysphagia was assessed with VFSS, were further evaluated with USG. It was observed that the findings from the USG indicating the severity of dysphagia were correlated (71). In our study, no significant difference was found between patients with SD and the healthy group in terms of USG evaluation. Although there was no statistically significant difference, it was observed that the geniohyoid muscle was larger in patients with spasmodic dysphonia, than in the healthy group'. If a sentence or statement is unclear, consider rephrasing it for clarity.It seems that there is a statistically significant difference in the geniohyoid muscle, in the results section.

Dysphagia may occur in patients with SD due to muscle involvement. Some studies have shown that this symptom can also develop secondary to Botox injection, which is the gold standard treatment. Although our patient group consisted of individuals, no complaints were observed after botox administration.

Study Limitations

The number of patients in our study is quite limited and in a larger group of patients this study would give more acceptable results. In addition, the study would be more comprehensive if videofluroscopic swallowing evaluation was performed in patients evaluated with FEES.

CONCLUSION

Even if they do not describe symptoms of swallowing dysfunction, their swallowing function may still be affected when compared to healthy individuals. Our patient group did not complain of dysphagia. FEES, EMG, and USG evaluation revealed no findings related to swallowing dysfunction. In addition, no change was observed in swallowing functions after botulinum toxin injection.

Ethics

Ethics Committee Approval: The University of Health Sciences Türkiye, Ankara Etlik City Hospital No. 1 Clinical Research Ethics Committee (decision number: AEŞH-EK1-2023-597, date: 04.10.2023) approved before the research began.

Informed Consent: We obtained informed consent from all participants.

Footnotes

Authorship Contributions

Surgical and Medical Practices: E.A., E.M.T., Concept: E.A., E.K.U., E.M.T., Design: E.A., E.K.U., Data Collection or Processing: E.A., E.B., E.K.U., E.M.T., Analysis or Interpretation: E.A., E.B., E.K.U., E.M.T., Literature Search: E.A., E.B., E.K.U., E.M.T., Writing: E.A., E.B., E.K.U., E.M.T.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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