The Laryngoscope

Botulinum Toxin Treatment of False Vocal Folds in Adductor Spasmodic Dysphonia: Functional Outcomes

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Objectives/Hypothesis: Supraglottic injection of botulinum toxin (Botox) has been described as an effective treatment for adductor spasmodic dysphonia (ADSD). Anecdotal evidence suggests that the patients have little to no breathiness after injection, but no formal longitudinal studies have been carried out to date. The purpose of this study was to examine the voice outcomes in patients with ADSD after supraglottic Botox injection.

Study Design: Retrospective case series.

Methods: Patients with ADSD who were treated with supraglottic Botox injections completed a qualitative self-evaluation of voice function after injection using the percentage of normal function (PNF) scale, a validated, quantitative scale from 0% (no function) to 100% (normal function). Posttreatment voice improvement after injection was determined using a Voice Handicap Index-10 (VHI-10) questionnaire.

Results: A total of 198 supraglottic injections were performed between July 2011 and October 2014. Twenty-five questionnaires were completed. Mean postinjection PNF was 95.0% $\pm$ 8.4% and was significantly increased from the preinjection mean PNF (62.5%) $\pm$ 22.6% ($P < 0.001$). The mean best VHI-10 for all injections was 7.23. In 19 of 25 patients (76%), there was no reduction in PNF in the early postinjection period. In the remaining six patients (24%), the decline in mean vocal function was 9.2%.

Conclusions: Supraglottic Botox injection is an effective treatment for ADSD. Postinjection voice is significantly improved, and the majority of patients do not experience breathy voice/decline in vocal function after injection.

Key Words: Adductor spasmodic dysphonia, botulinum toxin, false vocal folds, longitudinal functional outcomes, supraglottic, Botox.

Level of Evidence: 4.

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INTRODUCTION

Spasmodic dysphonia (SD) is a focal dystonia characterized by vocal task-specific action or intention-induced spasms. There are three classic types of SD. Adductor SD (ADSD) comprises 80% of the patients with the disorder. Abductor SD and patients with both adductor and abductor activity, mixed SD, comprise the remainder of the disease population. Diagnosis rests primarily on auditory-perceptual evaluation of connected speech supplemented by flexible nasopharyngolaryngeal examination.

The standard of care in the treatment of ADSD is injection of the affected muscles with botulinum toxin A (Botox), which causes a temporary chemical denervation of the thyroarytenoid-lateral cricoarytenoid muscle complex.[1] Consequently, patients experience smoother speech with fewer voice breaks. Unwanted effects of adductor muscle weakness may include loss of volume or breathiness of the voice. The initial breathy phase and the late declining phase where the spasms begin to return make up a considerable portion of the injection cycle and reduce the effectiveness of the treatment.[2] In addition, this has been shown to result in work impairment during the injection cycle.[3] Recently, a study was published examining the longitudinal functional outcomes of patients with ADSD treated with Botox injection of the thyroarytenoid muscle,[4] which gives good evidence to support the idea that an individuated dosing regimen helps minimize side effects and maximize functional and quality-of-life outcomes.

Using this study as a model, our aim is to study longitudinal functional outcomes in a similar patient population (i.e. those with ADSD) being treated with Botox injection into the false vocal folds as opposed to the thyroarytenoid muscle. This is also referred to as supraglottic Botox injection. Our institution has utilized supraglottic Botox in select patients since 1997. Advantages of supraglottic Botox injections include a more gradual onset of action, as well as a stabilization of vocal fold peaks and troughs associated with true vocal fold injections. Also, a less severe/absent breathy voice after injection has been observed, though not formally studied. Supraglottic Botox

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injections also seem to preserve singing voice/pitch control in many patients with ADSD as well.

Our objective is to examine the longitudinal effect of Botox treatment of the false vocal folds for ADSD, characterizing functional outcomes with the use of a self-reported questionnaire in which patients report the percentage of the normal function (PNF) of their voice after injection. Our hypothesis is Botox injection of the false vocal folds is an effective treatment for patients with ADSD patients and is associated with minimal vocal downtime (breathy voice) in the first 1 to 2 weeks after injection.

MATERIALS AND METHODS

Clinical records of all patients treated (University of Texas Health Science Center at San Antonio, Department of Otolaryngology–Head and Neck Surgery) with supraglottic botulinum toxin on a continuous basis from July 2011 through October 2014 were reviewed for inclusion in the study. The patient record was reviewed if a diagnosis of ADSD treated with supraglottic Botox injection was indicated.

All patients who presented for treatment of ADSD were asked to complete qualitative self-evaluation of voice function after Botox injection using the PNF scale, which provides a quantitative scale from 0% to 100% for the patients to rate their current functions in increments of five from 0% (no function) to 100% (normal function). The PNF was to be completed daily for the first 2 weeks and then weekly until next injection.[4]

In addition, all patients completed the Voice Handicap Index-10 (VHI-10)[5] when the best voice was achieved in the injection cycle. The VHI is comprised of a series of questions targeting the patients' perceptions of their own voices. It is a useful tool to help gain insight into the emotional, physical, and functional components of the voice problem as well as measure therapeutic outcomes.

Additional information on each injection was also recorded, including gender, age, injection technique, and dosage of Botox. Approval was obtained from our institutional review board prior to the commencement of the study.

At our center, patients are initially assessed and diagnosed based on history, laryngeal examination, and perceptual assessment of voice. Of those diagnosed with ADSD, the majority of patients receive electromyographic guided injection of the thyroarytenoid-lateral cricoarytenoid (TA/LCA) muscle complex. Professional voice users are offered supraglottic Botox injection as the initial approach if the vocal downtime from electromyography (EMG)-guided Botox could negatively impact their work-related vocal duties. In those patients intolerant of the postinjection breathy phase after standard EMG-guided injections, supraglottic Botox injections are offered as well. Patients normally receive a dose in the range of five to 10 units of Botox per false vocal fold, depending on their previous dose and results after the initial injection. All of the injections were performed in an outpatient clinic setting. All doses were delivered in a 4cc per 100 units of Botox dilution.

Patients undergoing a thyrohyoid (TH) approach for supraglottic Botox injection receive a small ($<$ 2 cc) injection of 1% lidocaine with 1:100,000 epinephrine into the skin overlying the thyrohyoid membrane and the deeper subcutaneous tissues. They also receive intranasal 2% tetracaine and oxymetazoline 0.05% sprays in preparation for the flexible transnasal laryngoscopy. The supraglottis and glottis are then visualized and anesthetized by dripping 5 to 6 ccs of 4% lidocaine through the side-channel of the laryngoscope via a catheter. Then, a 25-gauge needle is advanced through the thyrohyoid membrane and Botox is deposited in a submucosal plane, resulting in a characteristic wheal over the false vocal fold. A critical aspect of this injection is that the Botox is deposited in the submucosal space, resulting a ballooning of the mucosa and blanching of the injection area (Fig. 1).[6] Injections deposited deep to this plane result in greater chemodenervation and more variable and generally unfavorable results.

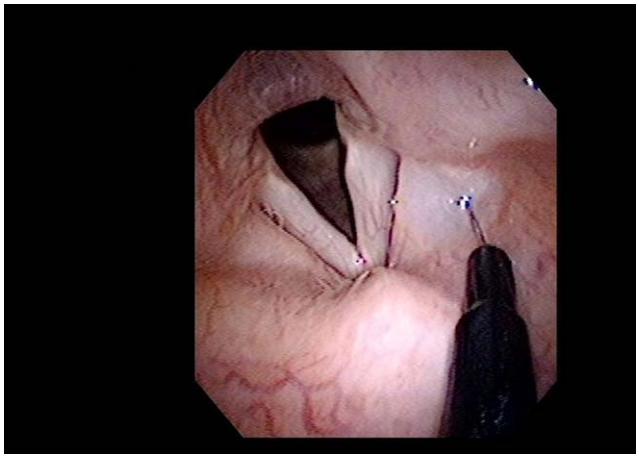

Fig. 1. Flexible laryngoscopy view of typical submucosal wheal after supraglottic Botox injection. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

Patients undergoing a peroral approach receive the same intranasal anesthetic/decongestant sprays as the TH group. The oral cavity and oropharynx are then anesthetized with a 1-second spray of Cetacaine. The supraglottis and glottis are then visualized and anesthetized by dripping 5 to 6 ccs of 4% lidocaine through a curved cannula placed perorally. The patient's tongue is grasped, and an orotracheal injector (Medtronic, Minneapolis, MN) with a 27-gauge needle is passed perorally. The needle is then visualized by the flexible laryngoscope and directed into the false vocal fold superficially, as in the TH approach.

A peroral approach is often attempted first. If the patient tolerates it well, we continue to use this approach for subsequent injections. For patients with increased gag reflexes, we often use a TH approach.

Statistical Methods

Continuously distributed outcomes were summarized as the mean plus or minus ($\pm$) one standard deviation and categorical outcomes with frequencies and percentages. The significance paired contrasts with regard to continuously distributed outcomes were assessed with the Wilcoxon signed rank sum test. We plotted the mean PNF versus time (days) from injection by subgroup and contrasted subgroups with regard to the mean PNF with repeated measures linear models of PNF in terms of subgroup, time, and the subgroup by time interaction, assuming an autoregressive order 1 autocorrelation matrix. All statistical testing was two-sided, with a significance level of 5%, and all analyses were carried out with R Version 3.1.2 (The R Foundation for Statistical Computing, 2013).

RESULTS

A total of 198 supraglottic injections were performed in 25 patients between July 2011 and October 2014. The mean age of the subjects was 62.6. Of those,

TABLE I.
Injection Approach.

	Female (N = 16)	Male (N = 9)	Total (N = 25)
Approach			
Peroral	14 (87.5)	3 (33.33)	17 (68)
Thyrohyoid	2 (12.5)	6 (66.67)	8 (32)
Total	16	9	25

Numbers in parentheses indicate percentage.

106 injections were performed in females and 92 were performed in males. The mean interval between injections was 109.5 days, with a mode of 84. The mean injected units/side was 7.2 per false vocal fold.

A total of 25 patients undergoing supraglottic Botox injections completed questionnaires. Of those, 16 (64%) were female and nine (36%) were male. Age range was 35 to 82, with a mean age of 59.4. All patients were treated with Botox injection of the bilateral false vocal folds. Seventeen patients (68%) underwent supraglottic Botox injection via a peroral approach, and eight (32%) underwent thyrohyoid approach (see Table I). A majority of females underwent a peroral approach, whereas a majority of males underwent a thyrohyoid approach. Five patients also underwent Botox injection of the strap muscles for essential tremor; however, this was a secondary diagnosis, so these patients were still included in the study.

The mean dose for all approaches was 7.56 units Botox per false vocal fold (FVF). The mean dose of Botox for the peroral approach was 7.81 ± 1.59 units/FVF, whereas the mean dose for the thyrohyoid approach was 7.03 ± 0.93 units/FVF. The range of botulinum toxin dosages was from four to 10 units/FVF. The mean dose for men was 6.94 ± 1.1 units/FVF, and in females the mean was 7.91 ± 1.52 units/FVF.

An assessment was carried out to determine if there was a *dip*, defined as a worsening in the PNF value below the baseline PNF, in the first 7 days after injection. This correlates to a worsening of the voice (generally a breathy quality) that is often reported after Botox injections for ADSD. In 19 of 25 patients (76%), there was no dip in self-reported vocal quality after injection. In the remaining six patients (24%), the decline in mean vocal function was 9.2%. The mean best VHI-10 for all injections was 7.23.

Mean postinjection PNF was $95.0\% \pm 8.4$ and was significantly increased from the preinjection mean PNF ($62.5\% \pm 22.6$) during the injection cycle ($P < 0.001$). The mean PNF over time, as measured in days postinjection, for all subjects is shown in Figure 2. Stratification by the presence or absence of a postinjection dip revealed variation in the PNF trajectories. The PNF trajectories determined by presence of a postinjection dip (yes, no) varied significantly ($P < 0.001$). Prior to day 42, the mean PNF in subjects without a dip was greater than the mean in those with a dip, and this orientation was reversed after day 42. Figures 3 and 4 show mean PNF by day postinjection with the presence of a dip and absence of a dip, respectively.

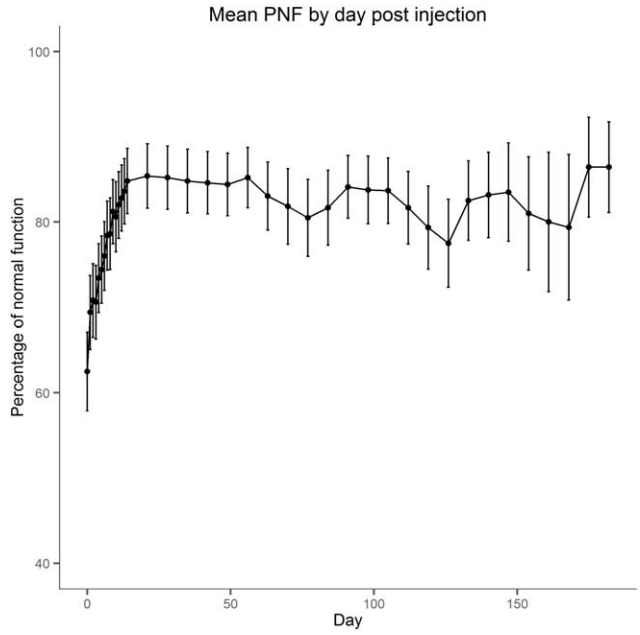

Fig. 2. Mean percentage of normal function by days postinjection in all subjects.

DISCUSSION

Our institution has utilized supraglottic Botox injections for select patients with ADSD since 1997. These patients, often professional voice users and singers, typically prefer the supraglottic approach for Botox injections due to the smoother onset of action and less breathy voice immediately after the injections. The percentage of patients with adductor spasmodic dysphonia

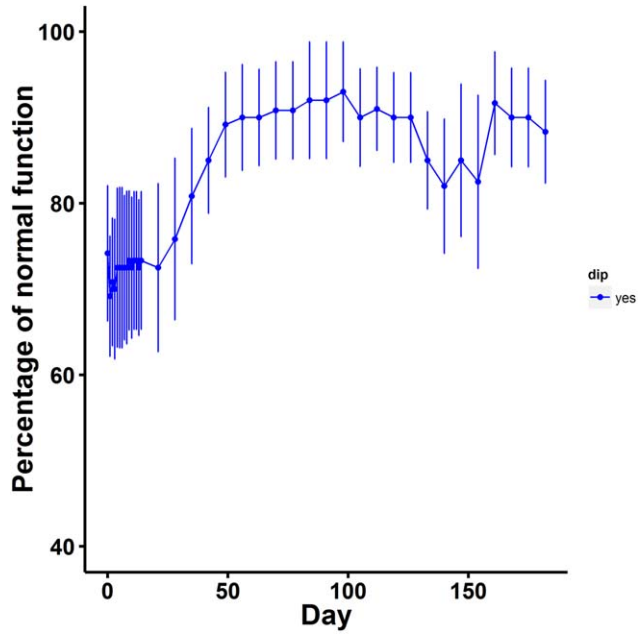

Fig. 3. Mean percentage of normal function by days after injection in those patients with a postinjection dip (n = 6). [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

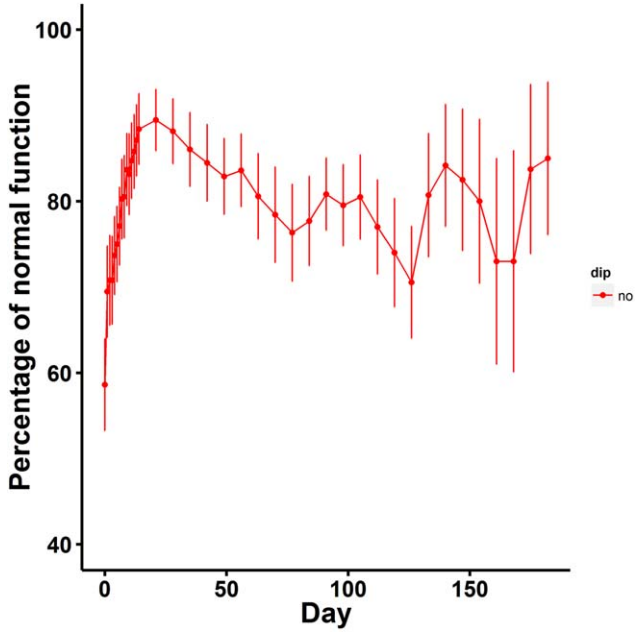

Fig. 4. Mean percentage of normal function by day after injection with no postinjection dip (n = 19). [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

in our practice who undergo supraglottic Botox injection (instead of standard EMG-guided TA/LCA injections) is roughly 20%. Although there are advantages to the technique, it takes a great deal longer to perform than an EMG-guided injection due to the time required to achieve local anesthesia to the laryngopharynx.

Our results show that with regard to mean PNF, supraglottic Botox injection for ADSD appears to be an appropriate and effective treatment. The majority of patients (74%) do not have the postinjection vocal decline, as measured by PNF over time. In those patients that demonstrate a decline in vocal function after injection, it is quite small (9.2% decrease in PNF). The maximal vocal results show a mean VHI-10 of 7.23, which is within the normal range. Anecdotally, we have suspected that supraglottic Botox injections last a shorter duration than EMG-guided injections; however, of the 198 supraglottic Botox injections studied, the mean interval time from one injection to the next was 109.5 days (around 15.6 weeks), with the most common interval of 84 days (12 weeks). This interval is comparable to intervals cited elsewhere in the literature for standard thyroarytenoid injections.[4] It should be noted that the diffusion pattern of the injected Botox in the supraglottis is not known. Due to the higher doses, there is undoubtedly broad diffusion to surrounding laryngeal musculature, and similar results could possibly be obtained with small doses into the TA/LCA muscles with EMG guidance, as was seen in a substantial number of patients injected in the study by Novokovic et al.[4]

There are case reports in the literature of the use of Botox injected into the false vocal folds for ventricular dysphonia[7] and muscle tension dysphonia,[8] as well an EMG-guided supraglottic injection for ADSD.[9] To our knowledge, however; this is the first case series of supraglottic Botox injection as primary treatment for adductor spasmodic dysphonia.

CONCLUSION

Supraglottic Botox injection for ADSD appears to be an appropriate and effective treatment. Mean postinjection PNF was 95.0% ± 8.4 and was significantly increased from the preinjection mean PNF (62.5% ± 22.6) during injection cycle ($P < 0.001$). The majority of patients (74%) did not have the postinjection vocal decline, as measured by PNF over time. In those patients who demonstrated a decline in vocal function after injection, it was quite small (9.2% decrease in PNF). The mean peak value for VHI-10 after injection was 7.23, consistent with a favorable postinjection vocal outcome.

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