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Transnasal Endoscopic Injection of Botulinum Toxin in Patients with Adductor Spasmodic Dysphonia

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Abstract

Introduction:

Adductor Spasmodic Dysphonia (ADSD) is the most common form of spasmodic dysphonia. It encompasses various symptoms affecting voice and speech. The objective of this study is to report the management of patients with ADSD using the transnasal endoscopic approach for laryngeal Botulinum Toxin (Botox) injection.

Materials and Methods:

A retrospective chart review of patients with ADSD who underwent transnasal endoscopic laryngeal Botox injection was conducted. Voice outcome measures included the Voice Handicap Index-10 (VHI-10) score and the degree of speech fluency.

Results:

Eight patients with ADSD who underwent 20 office-based transnasal endoscopic laryngeal Botox injections were included. The most commonly injected sites were the thyroarytenoid muscle (TA) and the false vocal fold in 95% and 55% of the cases, respectively. The mean dose of injected Botox was 2.48 ± 0.55 IU in the TA muscle, and 2.14 ± 0.53 IU in the false vocal fold. The mean amount of Botox injected in the larynx was 7.16 ± 2.42 IU. The mean follow-up period was 17.7 ± 13.3 months. There was marked improvement in speech fluency in 64.7% of the cases and mild improvement in one third of the cases. Marked improvement in speech fluency was recorded in 64.7% of the cases and mild improvement in one third of the cases. The mean VHI-10 score of patients dropped significantly from 22.47±4.08 to 15±4.69 following treatment ($p<0.001$).

Conclusions:

The transnasal endoscopic approach is an effective and well-tolerated approach for laryngeal Botox injection in patients with ADSD.

Keywords: Botox; Botulinum toxin; Hyperkinetic dysphonia; Spastic dysphonia.

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Introduction

Adductor Spasmodic Dysphonia (ADSD) is a complex form of voice disorder that affects a significant number of patients Risk factors include a positive family history and genetic predisposition with alteration in the DYT1 gene (1-3). Based on a study that included 169 patients with SD, stress and talking on the phone were also considered as aggravating factors in 47.3% of the cases (4). Patients with ADSD suffer from an array of symptoms such as voice breaks, difficulty in initiating speech, and an increase in phonatory effort. Voice tremor may also be present in 50% of the cases (5). Voice symptoms in patients with ADSD are mostly attributed to excessive tension in the vocal folds and supraglottic structures during phonation. Abnormal sensory gating and motor cortex inhibition lead to uninhibited laryngeal adductor reflexes and voice strangulation. In some patients, a delay between laryngeal muscle activity and the onset of phonation is often noted (6). Based on a radiologic study looking at brain structural changes in patients with spasmodic dysphonia (SD), Kostic *et al* noted the presence of alteration in the sensorimotor integration in addition to changes in corpus callosum, right caudate and putamen nuclei. The study was conducted on 43 participants, 13 with SD and 30 controls, using T1-eighted and diffusion tensor magnetic resonance imaging (7). In another study on brain activity in SD patients, Kiyuna *et al* reported changes in functional connectivity in the cerebellum-basal ganglia-thalamus-cortex loop. The authors concluded that the basal ganglia network plays an essential role in the pathophysiology of SD (8).

The treatment of ADSD is multidimensional involving various methods such as voice therapy, singing, psychotherapy, medication, and surgical intervention. The effective application of botulinum toxin (Botox) for managing focal dystonia in other body areas has fostered its use in patients with ADSD. Since its introduction by Blitzer *et al* in 1998 (6), laryngeal Botox injection has gained popularity among otolaryngologists as a reliable treatment for patients with ADSD. In a cohort of 900 patients treated with laryngeal Botox injection, significant improvement in voice symptoms was noted in 90% of the cases (6). Similarly, Patel *et al* reported a success rate of 88% in a cohort of 548 patients with ADSD who were treated with laryngeal Botox injections (9).

The effect of laryngeal Botox injection on voice varies across patients. In addition to patient-related factors such as degree of stress, level of education, and history of prior injections, there are procedure-related factors such as the dose of Botox injected, site of injection, and the technique used for injection. Laryngeal Botox injection can be performed using electromyographic (EMG) guidance, point-touch technique, trans-orally or trans-nasally. In 2016, in a systematic review of SD treatment which included 13 studies, Babette *et al* noted that 12 of the 13 studies described the use of laryngeal electromyography for laryngeal Botox injections (10). Research on the transnasal endoscopic approach for patients with ADSD is quite limited, with only three reports available in the literature (11-13). The objective of this investigation is to further highlight this technique by reporting the authors' experience in 20 cases. The surgical technique and added value of transnasal endoscopic laryngeal Botox injection are described.

Materials and Methods

Patients

After having obtained the Institutional Review Board approval (IRB ID: BIO-2022-0280), the medical charts and recording of patients who presented with ADSD to a tertiary referral center between August 2019 and July 2023, and having undergone office-based transnasal endoscopic laryngeal Botox injection was conducted (Botox®, Allergan Inc., Irvine, CA). The diagnosis of ADSD was based on the presence of delayed onset of phonation, voice breaks, strangulated voice and increase in vocal effort when the patient was asked to sustain a vowel and to count from 80 to 89. All patients had evidence of a harsh glottal attack and compression of the supraglottic laryngeal structures.

Data

Demographic data included age, gender, presence or absence of vocal tremor, site of injection, dose of Botox injected, and the number of injections. Voice outcome measures included the Voice Handicap Index-10 (VHI-10) score (14), and the degree of speech

fluency, which was rated by the physician after the injection as no change, mild improvement or marked improvement.

Surgical technique

While the patient was seated, the nasal cavities were anesthetized with sponges soaked in 1% lidocaine HCL and 1:100,000 epinephrine, that were left in place for 10 minutes. The oropharynx and hypopharynx were numbed using 2-3 sprays of 2% xylocaine. For the larynx, topical anesthesia was achieved by dripping 2 cc of 2% lidocaine HCL through the working channel of a flexible endoscope (Pentax Medical FNL-15RP3) while the patient sustained the vowel sound /eh/ (laryngeal gargle).

After successful application of local anesthesia to the nasal and laryngopharyngeal regions, a flexible nasopharyngoscope with a working channel was introduced through the nasal cavity into the larynx and positioned above the vocal folds. A 25-gauge flexible needle was then inserted into the working channel of the endoscope and guided to the mid-third of the vocal fold. A total of 0.1 cc, containing 2.5 IU of botulinum toxin type A, was injected into the thyroarytenoid muscle lateral to the vocal ligament under direct visualization (Fig. 1). Additionally, Botox was injected into the false vocal folds in 11 out of 20 cases (Fig. 2). The procedure was well tolerated by all patients, with no complications reported. Patients were advised to rest their voice for 24 hours post-injection to prevent displacement of the injected solution.

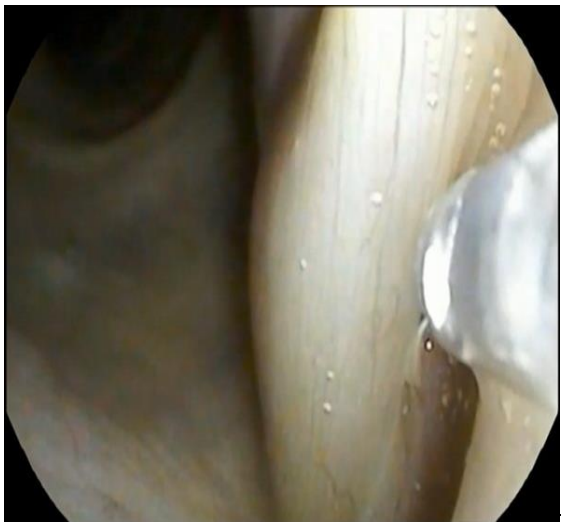

Fig. 1: Endoscopic image showing injection of botulinum toxin into the left thyroarytenoid muscle.

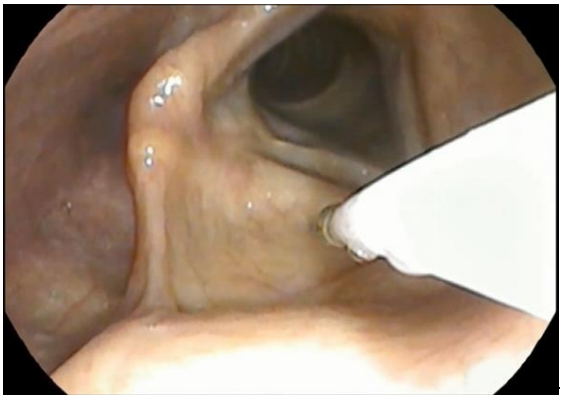

Fig. 2: Endoscopic image showing injection of botulinum toxin into the right false vocal fold.

Results

Eight patients with ADSD who underwent 20 office-based transnasal endoscopic laryngeal Botox injections were reviewed. The mean age of the study group was 68.1±10.3 years with a range of 57 to 83 years. The female-to-male ratio was 7:1. The mean number of procedures per patient was 2.5 ±1.85 and the interval between procedures ranged from 3 to 20 months with an average of 8.82 ±5.63 months. The total amount of Botox injected in the larynx ranged from 3.25 IU to 11.25 IU with an average of 7.16 ± 2.42 IU. In nineteen out of the 20 cases, injections were made in the TA muscle. The second most common injection site was the false vocal fold in 11 of the 20 procedures (55%). The mean dose of Botox injected in the TA muscle and false vocal folds was 2.48 ± 0.55 IU and 2.14 ± 0.53 IU respectively. Follow-up examination in 17 cases ranged from 3 weeks to 32 months with an average of 17.7 ± 13.3 months (Table 1).

Table 1: Patients and treatment characteristics

Age in years (mean ± SD)		**68.1±10.3**
Gender (n (%)) N=8 patients	Female	7 (87.5)
	Male	1 (12.5)
Presence of tremor (n (%))	With tremor	4 (50)
	Without tremor	4 (50)
Site of injection (n (%))	TA muscle	19 (95)
	False vocal folds	11 (55)
Number of injections (mean ± SD)		2.5±1.85
Mean dose injected ±SD	TA muscle	2.48±0.47
	False vocal folds	2.14±0.53

There was improvement in speech fluency following each injection. The improvement was noted as "marked improvement" in almost 2/3 (64.7%) of the cases and as "mild improvement" in one third of the cases. There was also a decrease in the VHI-10 score following laryngeal Botox injection in 14 of the 17 cases. The remaining three had no change in their VHI-10 score following injection. The average VHI-10 score of patients significantly dropped from 22.47±4.08 to 15±4.69 following treatment ($p<0.001$) **(**Table 2).

Table 2: Subjective voice outcome measures before and after Botox injection

Case	VHI-pre	VHI-post	Speech fluency
1	29	22	mild improvement
2	21	13	marked improvement
3	18	-	no follow-up
4	22	14	marked improvement
5	23	10	marked improvement
6	19	8	marked improvement
7	20	12	marked improvement
8	15	13	mild improvement
9	25	15	marked improvement
10	22	9	marked improvement
11	19	-	no follow-up
12	24	16	marked improvement
13	30	17	marked improvement
14	26	21	mild improvement
15	19	19	mild improvement
16	27	13	marked improvement
17	23	23	mild improvement
18	20	20	mild improvement
19	17	10	marked improvement
20	24	-	no follow-up

VHI: Voice Handicap Index

Discussion

The indication for the use of Botox in the head and neck area has increased exponentially over the years to include oromandibular dystonia, temporomandibular disorders, blepharospasm, hemifacial spasm, cervical dystonia, torticollis, and facial nerve synkinesis.

Botulinum toxin is also commonly injected into the cricopharyngeal muscle for the management of hyperfunction of the upper esophageal sphincter and in the veli palatine muscle for the treatment of palatal myoclonus. The success of Botox injection in treating focal dystonia in different parts of the body has paved the way for its use in patients with laryngeal movement disorders such as vocal tremor, vocal tics, and SD (15).

Laryngeal Botox injection under EMG guidance is the "Gold standard" technique used by most otolaryngologists in the management of patients with SD. Its effectiveness has been asserted in 2003 in a review by the American Association of Electrodiagnostic Medicine (16). The rationale behind the use of EMG during injection is to secure the proper placement of the needle within the targeted muscle before the injection is made. The position of the needle in the TA muscle is confirmed by the presence of distinct motor unit action potential (MUAP) while the patient is asked to sustain a vowel at a comfortable pitch and loudness.

Although laryngeal Botox injection under EMG guidance allows precision in injection, there are some limitations to this technique. Many otolaryngologists experience difficulty in inserting the needle with the electrode, and in interpreting the EMG signal. In addition, not all

otolaryngologists have access to an EMG machine in their clinic. To that end, an alternative technique such as the "point-touch technique" has gained popularity. The point touch technique relies on adequate identification of the laryngeal anatomical landmarks and good surgical dexterity. It is a blind procedure whereby the needle is inserted across the thyroid cartilage or the space between it and the cricoid cartilage. Green *et al* reported the successful use of this technique and improvement in speech fluency in 13 patients with SD up to six months post-injection. Ten of 11 patients who had upper airflow measures in that study had a decrease in their laryngeal resistance, and 3 out of 4 who had acoustic analysis had a decrease in jitter. The main complication post-injection was breathiness, which resolved within 2 weeks after the injection (17).

In 2014, Kim *et al* compared the treatment efficacy of percutaneous laryngeal Botox injection under fiberscope guidance vs. EMG guidance and reported no significant difference in outcome or in the duration of the effect of treatment. The study included 30 participants who were randomly allocated to either treatment modality and who were evaluated using the Voice Handicap Index (VHI) questionnaire in addition to acoustic and aerodynamic analysis (18).

The transoral approach is another technique less commonly used by otolaryngologists for laryngeal Botox injection in patients with SD. By indirect visualization of the larynx, the needle is inserted via the oral route into the thyroarytenoid muscle. The injection is given at two sites, antero-posteriorly and along the superior-inferior axis of the vocal fold. Ford *et al* reviewed 16 patients who underwent 1-4 injections with a mean of 4.5 units per patient. On a scale of 1 to 5 with 1 denoting an excellent voice and 5 a terrible voice, the authors reported a drop in the mean score from 4.4 pre-injection to 1.3 post-injection (19).

The success of the transoral approach was ascribed to the wide dispersion of the Botox when the injection is made under direct visualization and to the diffuse distribution of the motor end plate within the TA muscle (20). The authors recommended the use of this approach given its efficacy and the minimal discomfort experienced by patients during the injection. In 1996, Inagi *et al* examined the impact of variations in injection patterns on voice using the transoral technique and noted that laryngeal Botox injection within the TA/LCA complex yielded the best results and the shortest duration of adverse effect such as breathiness (21).

Transnasal endoscopic laryngeal injection of Botox is also a safe and effective alternative to the percutaneous and transoral approaches. In 1994, Rhew *et al* injected Botox into the TA muscles of 12 patients with ADSD using a flexible naso-pharyngoscope and noted a significant decrease in voice breaks and increase in sentence duration following the injection.[11] In 2009, in a short communication to the editor of the Journal of Laryngology and Otology, Hussein *et al* described transnasal laryngeal injection of Botox using a channel fiber-optic laryngoscope in an office setting. The procedure was well tolerated in 6 out of 7 patients with ADSD. No voice outcome measures were noted in their communication (9). In 2018, Kaderbay *et al* concurred with the use of the transnasal approach in-office for laryngeal Botox injection in the management of laryngeal movement disorders. The authors stressed the reliability of this approach which allows direct visualization and injection of various laryngeal structures ((13) Table 3).

The results of our study are in accord with the literature. There was improvement in speech fluency in all the cases and a decrease in the VHI-10 score following laryngeal Botox injection in 14 of the 17 cases. Moreover, the decrease in the mean VHI-10 score of the study group after treatment was significant ($p<0.001$). These findings and those of the literature support the use of the transnasal endoscopic approach for laryngeal Botox injection in patients with laryngeal movement disorders such as ADSD. The transnasal endoscopic approach allows the surgeon to navigate safely into the laryngopharyngeal complex and to place the needle with precision in the TA muscle under direct vision. Although this approach requires an assistant to do the injection, it is easy to perform and does not impose additional stress on the patient as the needle travels through the working channel of the endoscope. This is evidenced by the fact that the procedure was well tolerated by all the patients in our study group.

Table 3: Characteristics of previous studies reporting on transnasal Botox injection

Study	Number of patients	Diagnosis	Site	Dose	Number of procedures	Success rate	Side effects
Rhew et al (1994)	12	Adductor SD	TA muscle	6U for unilateral injections 2U for bilateral injections (total of 4U)	N/A	-Significant decrease in the number of voice breaks and sentence length. - No significant change in aperiodicity and fundamental frequency. -All patients reported significant improvement in tension and effort of speaking as well as decreased spasms and breaks.	-Mild dysphagia to liquids in 9 patients (for 14 days). - Excessive breathiness and decreased volume in 8 patients (for 23 days). -Abnormally high-pitched voice in 7 patients (for 69 days).
Hussain et al (2009)	7	Adductor SD	6 patients bilateral 1 patient unilateral TA muscle	range of 1.5U to 15U with an average of 2 to 4 units	70	N/A	Inability to tolerate fiberoptic laryngoscopy even with topical local anesthetic in 1 patient
Kaderbay et al (2018)	1	Unspecified laryngeal movement disorder	TA muscle (unilateral injection)	0.2ml at the desired concentration (not mentioned)	1	N/A	N/A

SD: Spasmodic Dysphonia; TA: Thyroarytenoid muscle; U: unit; N/A: Not Applicable

Conclusion

Transnasal endoscopic laryngeal Botox injection in patients with ADSD is an effective treatment modality in the majority of the cases. It is easy to perform and very well tolerated by patients. It allows direct visualization and injection of Botox within the true and false vocal folds. This approach does not entail the use of EMG guidance or well-skilled assistance.

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