

Botulinum Toxin Management of Spasmodic Dysphonia (Laryngeal Dystonia): A 12-Year Experience in More Than 900 Patients

Andrew Blitzer, MD, DDS; Mitchell F. Brin, MD; Celia F. Stewart, PhD

Objectives: This paper reviews a 12-year experience in more than 900 patients with spasmodic dysphonia who have been treated with botulinum toxin. **Study Design:** This is a retrospective analysis of patients with adductor spasmodic dysphonia (strain-strangled voice), abductor spasmodic dysphonia (whispering voice), and adductor breathing dystonia (paradoxical vocal fold motion), all of whom have been treated with botulinum toxin injections for relief of symptom. **Methods:** All of the patients were studied with a complete head and neck and neurologic examination; fiberoptic laryngostroboscopy; acoustic and aerodynamic measures; and a speech evaluation including the Universal spasmodic dysphonia rating scale. Some were given electromyography. All patients received botulinum toxin injections into the affected muscles under electromyographic guidance. **Results:** The adductor patients had an average benefit of 90% of normal function lasting an average of 15.1 weeks. The abductor patients had an average benefit of 66.7% of normal function lasting an average of 10.5 weeks. **Adverse effects** included mild breathiness and coughing on fluids in the adductor patients, and mild stridor in a few of the abductor patients. **Conclusion:** Botulinum toxin A injection of the laryngeal hyperfunctional muscles has been found over the past 12 years to be the treatment of choice to control the dystonic symptoms in most patients with spasmodic dysphonia.

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INTRODUCTION

Spasmodic dysphonia has become an area of major interest over the past decade, during which time major advances have been made in understanding the disorder, including improvements in its evaluation and major

changes in treatment. Spasmodic dysphonia, a focal laryngeal dystonia, is a chronic neurologic disorder of central motor processing characterized by action-induced spasms of the vocal folds. The vocal folds are normal at rest, but with an action-induced task-specific movement, the muscles contract inappropriately, causing abnormal movements and muscle spasms, typically resulting in dysphonia during speaking.¹⁻³

Historically spasmodic dysphonia ("spastic dysphonia") was considered a disorder of uncertain origin thought by many to be psychogenic, since patients often use sensory tricks (such as yawning or laughing when beginning to speak) to ameliorate the abnormal movements. Patients also report that their symptoms are worse when they are under emotional stress and are often better upon waking in the morning or after they have had an alcoholic drink. Many can laugh and sing normally. Symptoms are also usually worse when patients speak on the telephone.²

Spasmodic dysphonia presents most often as the adductor type, characterized by a strain-strangled voice that is harsh, often with a tremor, inappropriate pitch or pitch breaks, breathiness, and glottal fry. The less common abductor type is characterized by spasms of the posterior cricoarytenoid muscles, producing a breathy, effortful hypophonic voice with abrupt termination of voicing, causing aphonic or whispered segments of speech. Patients may also have a true mixed adductor-abductor type in which there is an admixture of breathy breaks and tight harsh sounds. Sometimes this is seen with compensatory behavior, but when one form is treated with botulinum toxin, the other gets much worse, so in these individuals, both adductor and abductor muscles require treatment. Cannito and Johnson⁴ proposed that both adductor and abductor abnormalities exist in all patients and that the symptoms depend on whether there is more adductor or abductor activity.

We have previously reported two other variations of presentation, *compensatory abductor dysphonia*, which is found in the group of adductors who produce a breathy voice by whispering or not contracting their vocal folds to prevent spasms and broken speech patterns; and much rarer *compensatory adductor dysphonia*, in which abduc-

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From the New York Center for Voice and Swallowing Disorders (A.B., M.F.B., C.F.S.), The Head and Neck Surgical Group, LLC (A.B., C.F.S.), the Department of Neurology, Mt. Sinai School of Medicine (M.F.B.), and the Department of Speech-Language Pathology and Audiology, New York University (C.F.S.), New York, New York.

Send Reprint Requests to Andrew Blitzer, MD, DDS, 425 West 59th Street, New York, NY 10019, U.S.A.

tor dysphonia patients try to prevent breathiness by beginning to speak with their vocal folds tightly contracted.¹⁻³ We have also described another entity termed *adductor breathing dystonia*, in which patients develop adductor spasms during breathing, producing paradoxical vocal fold motion. We reported 12 patients who have stridor and paradoxical vocal fold motion.⁵ They do not become hypoxic and the stridor abates when they fall asleep. A few of these patients also have other dystonic movements. Two of the patients had discoordination of the respiratory muscles on breathing, with paradoxical diaphragmatic movements as well as abnormal chest wall movements.⁶

The tremor activity found in patients with spasmodic dysphonia has been well described by Aronson et al.,⁷ who found that the tremor was similar to that found in patients with essential tremor. They also found that several of the patients had synchronous pharyngeal, lingual, velar, mandibular, facial, thoracic, and diaphragmatic tremor. Ludlow et al.⁸ also observed a vocal tremor that affected amplitude and wrote of a possible link between tremor and spasmodic dysphonia. Blitzler et al.⁹ studied spasmodic dysphonia with electromyography (EMG) and found that almost 25% of the patients had an irregular tremor of 4 to 8 Hz on phonation, with no resting tremor present. Another 6% had a regular tremor similar to that of essential tremor.

In 1982 Marsden and Sheehy first noticed that "all evidence points to the conclusion that blepharospasm and oromandibular dystonia seen in Meige disease is another manifestation of adult-onset torsion dystonia, [and] since dysphonia may occur in the same syndrome, it is quite likely that dysphonia itself may be the sole manifestation of dystonia."¹⁰ In 1984 our group recognized that the characteristics of "spastic dysphonia" were similar to the dysphonia found in some patients with generalized and multifocal dystonia. Both the clinical examination and EMG characteristics led us to the conclusion that most cases of dysphonia clinically diagnosed as spastic dysphonia are focal forms of cranial dystonia.^{1,9} Other focal forms include blepharospasm, torticollis, oromandibular dystonia, and occupational writer's cramp. We found that laryngeal dystonia may present focally or in association with other dystonic movements.² When the brains of dystonic patients have been studied pathologically, no consistent brain lesions have been found. However, most frequently mentioned lesions were found in the basal ganglia (putamen, head of the caudate, and the upper brain stem).¹¹ Hedreen stated that the circuit between the putamen and the striatopallido-thalamo-cortical area seems most likely to be involved.¹²

Symptoms of dystonia usually begin as focal dystonia involving a single region of the body. Patients with a diagnosis of dystonia are classified according to primary and secondary diagnosis. For a patient to have primary dystonia, there should not be any evidence by history, examination, or laboratory studies of any secondary cause for the dystonic symptoms, with the exception of precipitation by trauma. Therefore, there must be a normal perinatal and early developmental history, no prior history or neurologic illness or exposure to drugs known to cause acquired dystonia (e.g., phenothiazines). Results of intellectual, pyra-

midal, cerebellar, and sensory examinations and of diagnostic studies must also be normal. Spread to other regions is commonly seen in childhood-onset dystonia, while the disorder tends to remain focal with adult-onset. Of the patients who had primary laryngeal involvement, 16% had spread to another body part. These data suggest that patients should be advised of possible spread to another part and be followed and re-examined on a regular basis for signs of other dystonic involvement.²

Family history is also important: 12.1% of our series of primary laryngeal dystonia had a family history of dystonia.^{2,3} Over the past decade, significant advances have been made in our understanding of the genetics of dystonia and may prove to be a link to a cure or better treatment. Family linkage studies have identified several subtypes of dystonias with different genetic bases. In most cases of childhood onset, idiopathic dystonia, family studies show an autosomal dominant inheritance with reduced penetrance. A marker for some of the cases of childhood-onset dystonia has been found on chromosome 9.¹³ Other genes have been mapped for other phenotypes of the disease including an autosomal dominant dopa-responsive dystonia (DRD); X-linked Filipino torsion dystonia (XLTD); and an autosomal dominant (non-dopa-responsive) idiopathic torsion dystonia not mapping to the DTY1 gene on chromosome 9q34. Both the DRD and XLTD are rare forms of idiopathic torsion dystonia associated with parkinsonism.¹⁴⁻²⁰

The DTY1 gene was first identified in one large non-Jewish family with multiple members who have dystonia and has been found to be responsible for childhood-onset dystonia in the Jewish population.¹⁸ Both Jewish and non-Jewish families presented with the same symptom complexes. The dystonia characteristically begins in childhood or adolescence and starts in a limb. It has been postulated that different mutations in the DTY1 gene may be responsible for the difference between the Jewish and non-Jewish families, although this is unproven.²¹ Ozelius et al.¹⁸ reported linkage disequilibrium between haplotype ABL-ASS at the 9q loci and the DTY1 gene in the Ashkenazi Jewish population, suggesting that a single mutation in the DTY1 gene is responsible for many, if not all of the Jewish idiopathic torsion dystonia cases. In contrast, the late onset idiopathic torsion dystonias in the Ashkenazi Jewish population seem to be unrelated to this mutation; other mutations or genes are likely to be responsible.¹⁹ Linkage disequilibrium has not been reported in the non-Jewish population.²⁰

Nygaard et al.¹⁷ initially reported that the gene for the Segawa variant of dystonia (DRD) was on chromosome 14, at the appropriate locus, and a mutation in this gene is responsible for symptoms. Ichinose et al.²² further refined this observation and reported that a GTP-cyclohydrolase gene was mapped on chromosome 14q.

Botulinum toxin type A was developed by Alan Scott²³ in San Francisco as a treatment for strabismus and then for blepharospasm. Botulinum toxin is a potent neurotoxin that blocks the release of acetylcholine from the nerve endings at the neuromuscular junction. The light chain of the botulinum toxin type A acts as a zinc-dependent metalloprotease that specifically cleaves the SNAP-25 target pro-

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causing inhibition of synaptic acetylcholine-vesicle exocytosis in nerve endings.²⁴

The result is a dose-related muscle weakness that can be used therapeutically to treat focal dystonia, spasticity, gastrointestinal achalasia, hyperfunctional facial lines, tremor, and many other conditions related to overactivity of muscle. Historically, we gave the first laryngeal botulinum toxin injection of the vocal folds in April 1984. Both the Houston group²⁵ and the NIH group²⁶ then began botulinum toxin injections. The Houston and NIH group continued programs with large doses given unilaterally, to simulate the effects of the recurrent nerve section. We observed that bilateral injections permitted the use of smaller doses and produced better voicing. We postulated that if one vocal fold was immobile, the other vocal fold would have to compensate for it, and the dystonic symptoms in the functional vocal fold would be exaggerated, leading to poor voicing. Bilateral injections would be expected to address this problem, and should give better voicing results.

Other authors have suggested other approaches to toxin delivery. Ford et al.²⁷ reported an indirect laryngoscopic technique for injecting the vocal folds. They reported that the technique has the advantage of being "familiar to the otolaryngologist and requires no special [electromyographic] equipment or training." The onset of the response to toxin appears delayed (9.1 d), but the degree of benefit and the duration of efficacy appear comparable to the EMG-guided technique. In another technique described by Rhew et al.²⁸ the toxin injection was given through a needle placed via an operative channel of a flexible fiberoptic laryngoscope. The authors report satisfactory results.

METHODS

Initially all patients undergo a detailed head and neck examination, with particular attention for any spasms, dysfunction, or tremor of another area in the head and neck. Fiberoptic laryngoscopy and stroboscopy are performed in all patients to observe the glottal function for /i/, and then to look for disruptions, spasms, breathy breaks, and tremor while the patient speaks with connected speech segments. These movements can be video recorded and analyzed with slow speed and stop action. This examination cannot be easily performed with indirect laryngoscopy, because anterior tongue traction limits speaking ability. Eighty-seven percent of our patients had the adductor type of spasmodic dysphonia, characterized by a strain-strangled voice that is harsh, often with a tremor, inappropriate pitch breaks, breathiness, and glottal fry. The laryngostroboscopic examination of vocal function with connected speech segments is important for diagnosis. The stroboscope can help to define the nature of the associated tremor. We have used a variation of the staging system proposed by Koufman²⁹ and Morrison and Rammage.³⁰ Type 1 hyperadduction is forceful overcontraction at the vocal fold level with tight compression of the vocal processes and arytenoids. Type 2 is forceful contraction including contact of the false cords. In type 3 the thyroarytenoid muscle pulls the arytenoids anteriorly, narrowing the supraglottic airway. Type 4 is sphincteric closure, by where the arytenoids are pulled so far anteriorly that they tightly close against the epiglottis. These classifications are useful in describing the pretreatment phenomenology of the larynx.

In addition, 13% of our series have the abductor type of spasmodic dysphonia in which there are spasms of the posterior cricoarytenoid muscles, producing a breathy, effortful hypophonic voice with abrupt termination of voicing, causing aphonic or

whispered segments of speech. In patients with the abductor type, the laryngostroboscopic examination reveals a synchronous and untimely abduction of the true vocal fold that causes an extremely wide open glottic chink. The abductor spasms are triggered by consonant sounds, particularly when they are in the initial position in words. Having a patient say *taxi* or *Harry's hat* will often lead to an abnormal breathy break in speech.

Several of our patients also have a true mixed adductor-abductor type in which there is an admixture of breathy breaks and tight harsh sounds.

All of our patients also undergo a detailed neurologic examination. Patients are examined while performing postures and tasks that may bring out signs of dystonia, tremor disorder, or other neurologic disorders. A speech pathologist also makes acoustic and aerodynamic measures to evaluate for tremor, fundamental frequency, pitch and amplitude perturbation, harshness, fluency breaks, and breathiness.^{1,2}

Laryngeal EMG is performed in many patients to help evaluate tremor and areas of hyperactivity. Seventeen percent of the cases in our initial series had enlarged potentials, 4% had small potentials, and 6% had reduced numbers of motor potentials.⁹ Polyphasic potentials were found in 11% of the cases (perhaps showing a denervating and renerating process), and pseudomyotonic discharges and breaks in volitional activity were found in 2% each.⁹ Schaefer³¹ performed EMG that suggested involvement beyond the vagus nerve. If the EMG signal is put on the same time line as a voice spectrogram, a greater than normal delay in onset of sound production is observed, particularly in patients with the adductor variety.

Botulinum toxin A (BOTOX) is obtained from Allergan, Inc., in Irvine, CA. It is received as frozen, lyophilized toxin and is reconstituted with normal saline (without preservative) to a final concentration of 2.5 U/0.1 mL. The toxin is injected via a monopolar hollow-bore, Teflon-coated EMG needle connected to an EMG recorder. The patient is placed in the supine position with the neck extended. The needle is curved slightly to allow for a more anterior placement, and is placed through the neck skin and cricothyroid membrane into the thyroarytenoid muscle under EMG guidance. The patient is asked to phonate, and when the needle is in a very active area of the muscle, the toxin is injected. The patient is instructed to try not to cough or swallow when the needle is in the airway or in the thyroarytenoid muscle. The patient who has an uncontrollable cough is given 0.3 mL of 1% lidocaine injected through the cricothyroid membrane into the subglottic space. This usually causes the patient to cough, which distributes the anesthetic over the vocal fold mucosa. Anesthetic is not routinely given because it diminishes the EMG interference pattern, making the identification of the most active place in the muscle more difficult.^{2,3}

The results of our BOTOX injections were scored several ways. One score uses a subjective rating scale that has been used by our group since 1984. Patients, doctors, and the speech pathologist independently rate the patient's voice. The most conservative rating is used as the percentage of normal function—0 denotes no phonation and 100 denotes normal phonation. The patients rate themselves before injection, then every day for 2 weeks, and then weekly until their next injection. In addition, we have utilized a standardized vocal rating scale that has been validated in a multi-institutional study. Fifteen items are rated in a 1-to-7 scale (1 = normal, 2 = mild, 3 = mild/moderate, 4 = moderate, 5 = moderate/severe, 6 = severe, and 7 = very severe). The most significant items for the patients with abductor spasmodic dysphonia are the overall severity, breathy voice quality, aphonia, and tremor. These parameters are defined as:

1. Overall severity: the examiner's estimation of the degree to which overall speech calls attention to itself by its unusual, peculiar, or bizarre characteristics.³²

2. Breathy voice quality: breathy, weak, thin voice. Audible escape of air resulting in a thin, weak phonation, related to a functional inability to firmly adduct the vocal folds.³³
3. Aphonia: absence of a definable laryngeal tone. The voice is either severely breathy or whispered.³⁴
4. Voice tremor: tremulous or tremorous voice. Rapidly occurring fluctuations in pitch and/or loudness giving an impression of a tremulous voice.³³

Our first injection consisted of 2.5 U in one vocal fold. This injection had little effect, and we gave an additional 7.5 U, which caused a vocal fold paresis, a period of breathy dysphonia, and eventually a 90% improvement in vocal function. With our theory of exacerbating the dystonic symptoms on the functional vocal fold after unilateral weakness, and our goal of minimizing dose, we began bilateral dosing in most patients.

We continue to use the percutaneous technique of injection of the thyroarytenoid muscles that we have previously published. Since BOTOX therapy is symptomatic treatment, several strategies have emerged to try to give patients the best voicing, of the longest duration with the fewest side effects. Some patients are exquisitely sensitive to toxin, but do not have the best response to small bilateral doses, and have too much breathiness at larger doses. In these patients, we can stagger the larger doses, performing a unilateral injection, and giving the contralateral injection 2 weeks later. This allows for partial recovery before the second dose is given. Some patients prefer more frequent, small unilateral doses. In addition we have several patients who receive bilateral mini-doses (0.1–0.5 U) given more frequently. Although the duration of benefit in these patients is only 6 to 8 weeks, it avoids the breathiness in most of these patients.

After having very successful results using BOTOX to treat patients with adductor spasmodic dysphonia, in 1988 we attempted the first injection of a patient with abductor spasmodic dysphonia. The first patient was treated with BOTOX via direct laryngoscopy into one posterior cricoarytenoid muscle.³⁵ This was performed without EMG guidance, and little improvement was noted. Next, an EMG-guided, percutaneous technique was developed. The larynx is manually rotated away from the side of the intended injection, and the hollow-bore EMG needle with attached syringe is placed posterior to the posterior edge of the thyroid lamina. The needle is advanced through the inferior constrictor muscle to the cricoid cartilage and then moved out under EMG guidance to the optimum position in the posterior cricoarytenoid muscle. The patient is asked to sniff, which yields maximum abduction. The EMG signal is observed for correct placement, and then the BOTOX is injected in the area of brisk activity. An alternative technique may be used, particularly in young individuals with soft cartilage. After a small amount of 1% lidocaine is instilled in the subglottis, the EMG needle is placed through the cricothyroid membrane just above the cricoid cartilage anteriorly. The needle is advanced in this plane and then directed laterally, until it hits the rostrum of the cricoid cartilage. The cartilage is impaled and as the needle exits, there will be a big burst of potential from the electrical signal in the posterior cricoarytenoid muscle. The patient is instructed to sniff, and if the needle is in good position, the BOTOX solution is injected. In the older patient, this approach is very difficult owing to the calcification of the cartilage. We initially attempt to weaken or paralyze one posterior cricoarytenoid muscle with an injection of 3.75 U in 0.15 mL. We generally start with the muscle that appears to be most active on fiberoptic examination during phonation. In approximately 20% of our patients with abductor spasmodic dysphonia, weakening or paralyzing just one posterior cricoarytenoid muscle produces significant voice improvement. The other 80% need the other posterior cricoarytenoid to be injected. Conservative doses of 0.625 to 2.5 U in 0.1 mL are given into the contralateral pos-

terior cricoarytenoid, if the voice is not improved at 3 weeks from the first injection. The amount of toxin used in the second or third treatment is based on the amount of residual function of the first posterior cricoarytenoid injected, the adequacy of the airway, and whether the patient has had any respiratory symptoms. No further injections are given if there has been stridor or the glottic chink appears very narrow. To date none of our 130 patients with abductor spasmodic dysphonia have been intubated or tracheotomized related to treatment. The patients who have been injected but still have breathy breaks may need additional modalities added. Fifteen percent of our patients have been given small doses of systemic agents, including clonazepam, lorazepam, or baclofen. This combination has added benefit to most of the patients.³⁵

Some of the patients have had additional benefit with bilateral cricothyroid injections. In addition, 12 patients have undergone a type I thyroplasty to limit the abductor movement of one vocal fold. This technique in addition to toxin has improved the response in those 12 patients.³⁵

RESULTS

Of the 1448 cases of all dystonias seen by our group, 901 cases (62%) had vocal involvement. Of the 901 cases, 744 (82.5%) had primary dystonia and 157 (17.5%) had secondary dystonia (Table I). Of the primary group, 471 (63%) were female. This is similar to the female percentage (63.5%) seen in the group of all dystonias. The Jewish group was similar, with 20.4% of them having primary laryngeal dystonia. They were 27.8% of all primary dystonias. A positive family history was found in 12% of the patients with laryngeal dystonia.

In the group of 901 patients with laryngeal dystonia, 747 (82%) were of the adductor type and 154 (17%) were of the abductor type. Twelve (1%) had adductor breathing dystonia. The average age of onset was 39 years.

Treatment With Botulinum Toxin

Since we gave the world's first laryngeal botulinum toxin injection in April, 1984, we have injected 901 patients with toxin (Tables II and III). Because patients need multiple injections, this translates into 6300 injections over the past 13 years. The majority of the patients treated were of the adductor type (747 patients) and they collectively had 5314 injection sessions. The abductor type (154 patients) had 966 injection sessions. No patients in our series have developed resistance to toxin or antibody formation, and we are aware of no cases in the world's literature who have developed antibody at the low doses used for laryngeal injection.

Adductor Laryngeal Dystonia

Our dose range for the 13-year period was 0.005 to 30 U, with an average of 3.09 ± 3.1 . Our current average starting dose is 1 U per thyroarytenoid muscle. The doses are then modified to the patient's response. Some patients have staggered doses, others have unilateral small doses, and still others have mini-doses bilaterally, which are given more frequently. We developed these other strategies to try to maximize the patient's good voice. The breathy period can be minimized, but often more frequent dosing is needed. The average onset of effect was 2.4 days, with the peak effect at 9.0 days. The duration of benefit in the entire group was 15.1 weeks. The patients' initial rating av-

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TABLE I.
Laryngeal Dystonia.

	All Dystonia (n = 1448)		Laryngeal Dystonia (n = 901)	
	Primary	Secondary	Primary	Secondary
Number	1129	319	744	157
Age onset (±SD)	39.3 ± 17	37.0 ± 16.2	39.0 ± 16.2	40.1 ± 20.9
Female	717 (63.5%)	215 (67.4%)	471 (63.3%)	109 (69.4%)
Jewish	360 (27.8%)	74 (23.2%)	152 (20.4%)	33 (21.0%)
+ Fam history (%)	174 (15.4%)	24 (7.5%)	90 (12.1%)	14 (8.9%)
Focal (%)	740 (65.5%)	132 (41.4%)	492 (66.1%)	83 (52.9%)
Segmental cranial (%)	201 (17.8%)	51 (16.0%)	161 (21.6%)	32 (20.4%)
All segmental (%)	107 (9.5%)	60 (18.8%)	51 (6.9%)	17 (10.8%)
Generalized (%)	81 (7.2%)	76 (23.8%)	40 (5.4%)	25 (15.9%)

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eraged 52.4% function, with a final result after injection of 89.7% function with an average improvement of 37.3%.

The adverse effects from the laryngeal BOTOX injections included mild breathiness in 35% patients and mild choking on fluids in 15% of patients. Less than 1% had local pain or sore throat related to the injection, slight blood-tinged sputum, itch, or rash.

Nerve-Section-Failure Patients

Nine of the patients in the adductor series had failed a recurrent laryngeal nerve section. Four of the patients had more than one surgical procedure performed including Teflon injection and laser fold thinning. Laryngeal EMG was performed on all patients; most showed signs of chronic denervation with few and very small potentials. Others showed signs of reinnervation, perhaps from ansa cervicalis fibers, but there was tone and no volitional activity. Most of the recurrent laryngeal nerve section failures were treated unilaterally in the functional vocal fold with an average dose of 2 U. Some of the patients who had activity in the immobile vocal fold did well with the injection into that thyroarytenoid muscle. The results showed a functional rating of 81% when the mobile vocal fold was injected, and 60% when the immobile vocal fold was injected. Both groups did not do as well as those patients who never had surgery, who averaged better than 90% of normal function.

Anterior Commissure Release

We have treated three patients who failed an anterior commissure release procedure (Tucker procedure). In these patients the larynx appeared foreshortened, but the adductor spasms were as intense as in the nonoperated

group. These patients were much more difficult to treat, since there was significant scar tissue in the cricothyroid membrane are, and in the anterior vocal fold. These patients required larger doses than the average patient with adductor spasmodic dysphonia, perhaps because of the barriers to diffusion related to scarring. Although the spasms could be reduced in this group, most noticed a weakened voice with limited pitch range. They also had an extended hypophonia after injection.

Adductor Breathing Dystonia

Based on the benefit seen in the adductor group who were injected with BOTOX, we attempted to reduce the symptomatic adductor breathing spasms with similar doses. Patients received between 0.625 and 3.75 U in each thyroarytenoid muscle, depending on the severity of the spasms. Patients used a rating scale based on percent of normal function relating to the severity of their breathing. The average preinjection function was 27% and pulmonary function tests showed abnormal flow volume loops with intermittent interruptions of airflow during inspiration or expiration in 20 of 24 patients. Most of the patients also had diaphragmatic dysfunction on testing. The average best postinjection function was 82% of normal, making the average percentage improvement 55% (P = .0001). The mean duration of relief from the stridor was 14 weeks (range, 6–26 w). A breathy voice lasting 1 to 2 weeks occurred in 50% of the patients. Mild choking on fluids also occurred in 5 of 12 patients lasting 1 week.

Abductor Spasmodic Dysphonia

Since 1989 we have treated 154 abductor dysphonic patients, with an average age of onset of 39 years.³⁵ After

TABLE II.
Botulinum Toxin Treatment.

Laryngeal Spasms	No.	Visits (n)	Dose Injection Per Session	Onset of Effect (d)	Peak Effect (d)	Duration Benefit (w)	Percent of Normal Function		
							Initial	Final	Final-Initial
Adductor	639	4621	3.096 ± 3.1 (.005–30)	2.4 ± 4.3	9.0 ± 12.7	15.1 ± 12.3	52.4 ± 22.0	89.7 ± 13.0	37.3 ± 20.7
Abductor	108	840	2.163 ± 1.07 (0.5–6.25)	4.1 ± 5.5	10.0 ± 12.5	10.5 ± 12.2	54.8 ± 21.9	66.7 ± 23.4	16.3 ± 11.7

evaluation the patients are started with 3.75 U injected into the most active posterior cricoarytenoid muscle. Of the 154 patients, 31 (20%) developed a good voice without breathy breaks. The others all needed additional toxin injected in the contralateral posterior cricoarytenoid in doses ranging from 0.625 to 2.5 U. The muscles were titrated based on symptom, fiberoptic evaluation of motion and the airway, and whether the patient developed noisy breathing or stridor. The average onset of effect was 4.1 days, with the peak effect at 10.0 days. The duration of benefit was 10.5 weeks. Patients initially rated themselves at 54.8% of normal function and improved to an average of 66.7% of normal function. Nine patients received injections of 2.5 U in each cricothyroid muscle in addition to the posterior cricoarytenoid injections. These were patients who, despite significant limitation of abduction, still had breathy breaks and/or tremor. This technique was based on the work of Ludlow et al.,³⁶ who found significant abnormal activity in the cricothyroid muscle on EMG. Of these nine patients, five had benefit with louder voice with fewer breaks. One patient actually got worse with this injection, and we postulated that the cricothyroid was actually involved in a compensatory strategy, and that with the muscle weakened, the abductor spasms were less well controlled. In addition, 10 patients had unilateral type I thyroplasty, to mechanically limit the amount of abduction of one vocal fold. This combination of BOTOX and thyroplasty raised the best average percentage of function to 82% of normal.

When our group of patients with abductor spasmodic dysphonia is analyzed, 30% have tremor and 46% had abductor spasmodic dysphonia in addition to segmental cranial or axial dystonia. Some of these had respiratory muscle involvement. The highest percentage improvement was in the group with focal laryngeal involvement without tremor. They had an average of 43% improvement of normal function, with an average best function of 80%. The worst response was in the group with combined dystonic abnormalities, with only a 30% improvement.

Adverse experiences included four patients who developed exertional wheezing/stridor when going up stairs or jogging and 10 patients who reported some dysphagia. The dysphagia is probably related to some of the toxin diffusing into the inferior constrictor muscle. These side effects have been transient, usually resolving within 1 week.

DISCUSSION

Spasmodic dysphonia, a focal dystonia affecting the larynx, is a disorder of central motor processing. It produces adductor spasms with strain-strangled voice in 87% of patients, abductor spasms with hypophonia and breathy breaks in 12%, and paradoxical vocal fold motion for breathing in 1%. Sixteen percent of the patients with primary laryngeal involvement go on to have another part involved with the dystonia. Twelve percent have a positive family history for dystonia.

As with other dystonic conditions, botulinum toxin intramuscular injections have been found to be very useful in the management of the muscular spasms produced by central motor processing abnormalities. Over the past

13 years we have treated 901 patients who have spasmodic dysphonia, translating to 6300 injections. Most of the patients treated had adductor spasmodic dysphonia and the majority had bilateral injections of 1 U or less, producing an effect in 2.4 days and achieving nearly a 90% rating of normal function, and lasting 15 weeks. There was mild breathiness in 35% of the patients for less than 1 week, with 15% having mild coughing on drinking fluids. Patients with spasmodic dysphonia who have failed recurrent nerve section or anterior commissure release also benefit from botulinum toxin injections, but do not have as good a result as those who have not had any anatomical changes made. Patients with adductor breathing dystonia also found significant improvement with botulinum toxin injections to an average of 82% of normal breathing.

The patients with abductor spasmodic dysphonia also showed benefit from toxin injection. To avoid stridor and dyspnea, we have developed a strategy of injecting one posterior cricoarytenoid muscle with 3.75 U of BOTOX. The symptoms will abate in 20% of the patients, and the other patients are re-evaluated in 2 weeks. If they do not have any respiratory symptoms, and they continue to have breathy breaks and hypophonia, they get additional toxin injection on the contralateral side of 0.6 to 2.5 U. The dose is related to the amount of spasm and their airway status. We found the average onset of toxin effect in the group was at 4.1 days, with a peak effect at 10 days and an average duration of benefit of 10.5 weeks. The patients achieved a benefit to 66.7% of normal function. Thirty percent of these patients received additional systemic agents including clonazepam, trihexyphenidyl, or baclofen. Others had type I thyroplasty to limit the excursion of the vocal fold. A few patients experienced mild stridor or dysphagia to solids that resolved in 1 week.

The injections are performed on an ambulatory basis with little discomfort. Graded weakening can be achieved by using low doses initially, and then repeating injections to achieve the optimum weakness desired. After iterating these doses, one is able to determine the proper dose for future injections. If too much weakness is produced, the strength gradually returns with time. There is a learning curve in obtaining consistently good responses with small doses and few side effects, as noted by our continued downward trend in dosing, and our ever-increasing benefit ratio.

CONCLUSION

Spasmodic dysphonia has been shown to be a laryngeal dystonia that is a disorder of central motor processing. It causes vocal fold adductor spasms in 87% of patients in our series, producing predominantly a characteristic strain-strangled voice. In 13% it produced primarily abductor spasms, producing hypophonic voice with breathy or aphonic speech segments. In a small number of patients it produces adductor breathing dystonia, in which there is a paradoxical vocal fold motion and stridor. The most effective therapy for most patients is local treatment, since central control of symptoms has been disappointing. Botulinum toxin A (BOTOX) injection of the laryngeal hyperfunctional muscles has been found over the past 12 years

to be the treatment of choice to control the dystonic symptoms in most patients with spasmodic dysphonia.

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