Botulinum Toxin in the Management of Laryngeal Tics

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Summary: The objective of the study was to demonstrate the utility of botulinum toxin (BTX; Botox: Allergan Pharmaceuticals, Irvine, CA) type A injections for symptom reduction in laryngeal tics. The study consisted of case studies and literature review. Case histories of two patients with laryngeal tics are presented. Treatment was administered using BTX type A injected into the thyroarytenoid muscles using electromyographic guidance or via direct laryngoscopy. Treatment outcomes were measured using clinical rating scales with a range from 0 (no response) to 4 (maximal response). A subjective assessment of reduction in premonitory sensations was recorded. Subject 1 was a 49-year-old female with onset of laryngeal tic (throat clearing) at 46 years. She received six injections over 24 months. The lowest effective dose was 1.25 units bilaterally, producing complete resolution of the tic behavior (peak effect of 4/4) and reduction of the premonitory sensations. The median duration of benefit was 13 weeks. Subject 2 was a 14-year-old male with Gilles de la Tourette syndrome with laryngeal symptoms including throat clearing, barking, and crowing. He received three injections, with the lowest effective dose of 0.625 units bilaterally. He achieved marked reduction (peak effect of 3/4) of the throat clearing, barking, and crowing behaviors. There was also substantial reduction of the premonitory sensations. The median duration of benefit was 10 weeks. The cases presented herein are examples of successful treatment with low-dose BTX type A to reduce the symptoms of laryngeal tics, leading to improved quality of life. These cases add to the relatively small number of similar patients reported in the literature, and support the use of chemical neuromuscular blockade for treatment of laryngeal tic symptoms.

Key Words: Tics—Larynx—Botulinum toxin—Tourette syndrome.

INTRODUCTION

Laryngeal tics are some of the most distressing manifestations of tic disorders. Also called vocal or phonic tics, these symptoms can vary in severity from repetitive throat clearing, barking, grunting, or sniffing to much more complex utterances such as screaming, coprolalia, echolalia (repeating other people’s words), or palilalia (repeating one’s own words).1 As with other tic symptoms, patients with laryngeal tics report a strong premonitory urge that is relieved by the behavior. The presence of these
uncontrollable behaviors can create a substantial negative impact on a patient’s quality of life, contributing to social isolation, performance problems in school or work, or difficulties with activities of daily living.

Treatment of laryngeal tics can be challenging. As a rule, laryngeal tics are treated systemically in the context of more widespread tics, usually in patients with Gilles de la Tourette syndrome. Medical regimens may include antidopaminergic agents, haloperidol, pimozide, tetrabenazine, clonidine, and fluphenazine. Other psychoactive agents may be used for associated conditions such as obsessive-compulsive disorder or attention deficit disorder, which are frequent comorbidities in tic patients. The side effects of all these centrally acting medications can be quite substantial, including tardive dyskinesia, hepatotoxicity, sedation, weight gain, and QT prolongation on electrocardiogram. Moreover, psychostimulants to address some coincident psychiatric conditions may worsen tic behaviors. Some patients on medical regimens have reported worsening of laryngeal tics even when body tics are improved.

In the past decade, several reports have appeared in which botulinum toxin (BTX; Botox: Allergan Pharmaceuticals, Irvine, CA) type A has been used successfully in the management of simple motor tics. In total, a relatively small number of patients with laryngeal tics have been reported, but treatment outcomes have been very favorable, with reduction of laryngeal tics in over 90% of patients and with reduction of premonitory urges.

The purpose of this report is to describe the treatment approach and outcome in two patients with laryngeal tics. In each case, the minimum effective dose of BTX was sought to reduce tic behaviors while still minimizing side effects of the injections. The goal of therapy was to ameliorate the tic behaviors such that the subjects would be able to (1) experience an improvement in their overall ability to function in their daily life and (2) reduce or eliminate their dependence on systemic tic medications if possible.

**METHODS**

For each subject the following data were collected: age at onset of laryngeal tics, duration of symptoms prior to first BTX injection, phenomenology of tic behaviors, and previous therapy trials with outcomes and side effects. Five-level subjective scales, each scored 0–4, were used to rate the peak effect of BTX, reduction of premonitory urges after therapy with BTX, and disability attributed to the tics before and after BTX (Table 1). Duration of perceived benefit and the side effects of BTX were recorded after each injection. In analysis of results, where applicable, median values are presented because the data are not normally distributed.

BTX type A was used for all intramuscular injections. The target muscle was the thyroarytenoid, either unilaterally or bilaterally, using electromyographic guidance (Medtronic AccuGuide Muscle Injection Monitor with computer interface: Medtronic-Xomed Surgical, Jacksonville, FL) or under direct vision via direct laryngoscopy using an orotracheal injector system (Medtronic-Xomed Surgical). The site and dosage of each BTX injection were recorded.

**Case 1**

Subject 1 was a 49-year-old female with no other medical history who presented for evaluation of 3 years of chronic throat clearing. Symptoms had initially been attributed to upper airway allergy.

**TABLE 1. Rating Scales**

<table>
<thead>
<tr>
<th>Peak effect of BTX</th>
<th>Reduction of premonitory urge</th>
<th>Disability caused by laryngeal tics</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 = No effect</td>
<td>0 = Less than 25%</td>
<td>0 = No disability</td>
</tr>
<tr>
<td>1 = Mild effect but no functional improvement</td>
<td>1 = 25–49%</td>
<td>1 = Minimal impact</td>
</tr>
<tr>
<td>2 = Moderate effect but no functional improvement</td>
<td>2 = 50–75%</td>
<td>2 = Moderate impact</td>
</tr>
<tr>
<td>3 = Moderate change in both severity and function</td>
<td>3 = 76–99%</td>
<td>3 = Major impact</td>
</tr>
<tr>
<td>4 = Marked improvement in both severity and function</td>
<td>4 = 100%</td>
<td>4 = Debilitating</td>
</tr>
</tbody>
</table>
behavior had become steadily more persistent, progressing to a constant and uncontrollable loud forceful expiratory noise that occurred many times per minute and was exacerbated by stress or anxiety. She described a strong premonitory sensation of mucus in the throat that was briefly relieved by the behavior. The symptom was affecting her ability to work as an executive secretary and had become very distracting to others and to the patient herself. Treatment trials had included histamine type 2 receptor blockers, proton pump inhibitors, systemic and topical antihistamines, inhaled steroids and bronchodilators, antibiotics, allergy immunotherapy, and benzodiazepines. At the time of her initial evaluation in our clinic, she was being managed with a nasal steroid, two systemic antihistamines, clonazepam, and allergy immunotherapy. Her symptoms continued unabated, and she had side effects of sedation and mucosal dryness, the latter of which seemed to exacerbate the throat clearing. Complete head and neck examination including nasal and laryngeal endoscopy revealed no abnormalities of structure or function. Neurologic examination was unrevealing. Diagnosis of laryngeal tic was made based on the nature of her symptoms, lack of improvement with medical trials, and lack of any apparent pathology on examination. She was treated with BTX using electromyographic guidance, as detailed in Table 2.

**Case 2**

Subject 2 was a 14-year-old male with almost lifelong tic symptoms. Symptoms had first appeared at 2 years of age with blinking, shrugging, and wrinkling of the nose. By the age of 7 years, he had developed arm twitches and barking vocal tics, which led to the diagnosis of Tourette syndrome. The intensity and frequency of the tics had increased over the years, leading to multiple trials of medical therapy with neuroleptic medications, with only partial relief of body tics and vocal tics. He experienced side effects of sedation and blunting of his normal affect, and had missed numerous days of school each year. He required therapy with antidepressants and anxiolytics for much of his later childhood and early adolescence. As a teenager, he began to experience major social anxiety, and developed features of obsessive-compulsive disorder. Despite these challenges, he maintained good academic performance. Upon referral to our clinic, he exhibited clicking, throat clearing, barking, and crowing vocal tics. The vocal tics occurred almost constantly and were worsened by attempts to voluntarily suppress them. He had grimacing and blinking behaviors also. He was being managed with haloperidol and venlafaxine. He had recently seen a neurologist for a trial of BTX therapy for shoulder shrugging, and had achieved substantial relief in that regard.

### TABLE 2. Subject 1, 49-year-old Female With Throat Clearing Tic

<table>
<thead>
<tr>
<th>Date (mo/y)</th>
<th>BTX Dose (units) and Location*</th>
<th>Peak Effect (0–4)</th>
<th>Duration of Benefit (Weeks)</th>
<th>Reduction of Urge to Tic (0–4)</th>
<th>Side Effects</th>
<th>Disability Before Injection (0–4)</th>
<th>Disability During Benefit Interval (0–4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10/03</td>
<td>1.25 Right</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>None</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>11/03</td>
<td>1.25 Left</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>Slight dysphonia with singing</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>3/04</td>
<td>1.25 Both</td>
<td>4</td>
<td>12</td>
<td>3</td>
<td>Breathy × 10 days, mild dysphagia</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>7/04</td>
<td>1.25 Both</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>Minimal breathiness</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>8/04</td>
<td>1.25 Both</td>
<td>4</td>
<td>14</td>
<td>3</td>
<td>Breathy × 7 days, mild dysphagia</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>1/05</td>
<td>2.5 Right, 1.25 Left</td>
<td>4</td>
<td>&gt; 52</td>
<td>3</td>
<td>Breathy × 30 days, but able to work. Not able to sing for 3 months. No dysphagia</td>
<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>

*Thyroarytenoid muscle(s).
and neck examination including laryngeal endoscopy was unrevealing. Because of his level of anxiety about injections, BTX was administered under a brief general anesthetic via operative laryngoscopy with injection of the thyroarytenoid muscles under direct vision, as detailed in Table 3.

RESULTS

Case 1

Subject 1 had experienced onset of laryngeal tic symptoms at age 46, 3 years prior to the first BTX injection. Her self-rated disability prior to her first BTX injection was level 3. She received two initial unilateral doses of BTX that were below the threshold of effectiveness for her, with neither benefit nor detrimental side effects produced. She then received a total of four effective injections of BTX, with the lowest effective dose being 1.25 units BTX per thyroarytenoid muscle. For the four effective injections, the median peak effect was 4 (range 1–4), and the median reduction in premonitory urge sensation was 3 (range 1–3). The median duration of benefit was 13 weeks (range 2–52 weeks). Side effects included breathy phonation for a median of 8.5 days (range 0–30 days) and minimal dysphagia. The median self-rated disability prior to injection was 2.5 (range 2–3), and the median disability during the interval of perceived benefit after injection was 0 (range 0–1). After the first effective injection, she was able to discontinue clonazepam successfully, though she did continue to use nasal steroids and systemic antihistamines for control of pre-existent allergic rhinitis.

Case 2

Subject 2 experienced onset of vocal tics at 7 years of age, which was 7 years prior to the first BTX injection. His self-rated disability prior to the first BTX injection was 4. To date, he has received a total of three injections of BTX to the thyroarytenoid muscles bilaterally in varying doses. For the first injection, a low dose of 0.625 units bilaterally was chosen, producing a peak effect of 3, and a reduction in premonitory urge of 3. Duration of benefit was 8 weeks. He experienced 7 days of breathy phonation without dysphagia. For subsequent injections, dosage was increased in an attempt to prolong the duration of benefit. The last injection was 1.875 units bilaterally, and produced 8 days of breathy phonation without dysphagia, with perceived benefit lasting 11 weeks. Overall, for the three injections the median self-rated disability prior to injection was 3, and the median disability during the interval of perceived benefit was 1.

Interestingly, Subject 2 also experienced significant anxiety in the first 4 days after the first injection. This was attributed to the initial persistence of the premonitory urge and his inability to relieve the sensation because the muscles normally used in

<table>
<thead>
<tr>
<th>Date (mo/y)</th>
<th>BTX Dose (units) and Location*</th>
<th>Peak Effect (0–4)</th>
<th>Duration of Benefit (Weeks)</th>
<th>Reduction of Urge to Tic (0–4)</th>
<th>Side Effects</th>
<th>Disability Before Injection (0–4)</th>
<th>Disability During Benefit Interval (0–4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8/05</td>
<td>0.625 Both</td>
<td>3</td>
<td>8</td>
<td>3</td>
<td>Hoarse × 7 days, no dysphagia. Anxiety due to initial increase in urge to tic; alprazolam × 7 days</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>11/05</td>
<td>1.25 Both</td>
<td>3</td>
<td>10</td>
<td>3</td>
<td>Hoarse × 10 days, no dysphagia. Less anxiety after injection: alprazolam for 3–4 days</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>2/06</td>
<td>1.875 Both</td>
<td>3</td>
<td>11</td>
<td>3</td>
<td>Hoarse × 8 days, no dysphagia. No anxiolytics required</td>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>

*Thyroarytenoid muscle(s).
the tic behavior were weaker. He was managed with alprazolam 0.25 mg every 8 hours as needed, but he was able to discontinue the medication after the seventh day. The anxiety response lessened with each subsequent injection, and he did not require any anxiolytics after the third injection.

Subject 2 was able to discontinue haloperidol and venlafaxine after the second BTX injection. His parents stated that his affect improved and that he was able to complete the school year with no absences, giving him the longest interval of continuous school attendance since the second grade.

**DISCUSSION**

Several reports over the last decade have supported the use of BTX in the management of tic disorders.2–9 Tics comprise brief movements (motor tics) or sounds (vocal or phonic tics) that occur intermittently and unpredictably out of a background of normal motor activity, and may occur as isolated (simple) tics or complex sequences.1 Tics are most often associated with the Gilles de la Tourette syndrome, but they can also occur spontaneously or in association with other conditions.1 Tic behaviors are accompanied by a premonitory sensation described as an urge or feeling that is relieved by the motor or phonic behavior. Medical therapy is considered the first line of treatment for tic behaviors, typically relying on neuroleptic medications.2–4 Due to the severity of their side effects, these medications can be of limited usefulness; moreover, they are not always effective, and some have reported worsening of vocal tics even when there is improvement of other motor tics.5 BTX is theorized to lessen tic behaviors both by weakening muscles involved in the tic behavior and by reducing the premonitory urge that drives the behavior, possibly by reducing resting isometric tone in affected muscles.10

Previous reports on the use of BTX in laryngeal tics comprise a total of less than 40 subjects.4–6,8,9 The largest group of subjects was reported by Porta et al.6 They reported on results of BTX injections for phonic tics in 30 patients with Tourette syndrome, all of whom received 2.5 units BTX to the thyroarytenoid muscles bilaterally over 12 months (mean of 1.9 injections over 12 months, range 1–5 injections). Over the 12-month interval, 93% of patients reported improvement from BTX therapy. The mean duration of response for all subjects was 102 days (14.6 weeks) with a range of 20–300 days. Their patients achieved a decrease in premonitory experiences, with 53% reporting sensations before therapy and only 20% after treatment. The only reported side effect of BTX was hypophonia that occurred in 80% of patients.

Other studies that have addressed management of laryngeal tic patients report a total of seven additional patients treated with BTX.4,5,8,9 In an excellent study of the utility of BTX in tic disorders, Kwak et al4 reported results of therapy in 35 patients with various tic manifestations. Of these patients, four were treated for vocal tics. They were treated with high dose BTX to the vocal cords (muscles not specified) using 17.8 ± 6.5 units. Although the specific responses to therapy for the vocal tics were not outlined, it was stated that all patients experienced hypophonia, but that the vocal tics “responded very well.” Three other authors have described BTX therapy for vocal tics in one patient each, all of whom achieved improvement in quality of life due to reduction in the tic behavior.5,8,9

The approach to dosing BTX in the current report was to determine the lowest effective dose for each subject. By using this approach, side effects of the BTX injections were minimal and short lived, and caused very little inconvenience to the subjects. The disadvantage of low-dose therapy is the potential for shorter duration of therapy, but the typical duration of therapy for most of the injections reported here was 8–14 weeks, consistent with results in the literature. Subject 1 had one injection that was only effective for 2 weeks, probably due to placement of BTX in less active areas of the thyroarytenoid muscle. However, the same subject also experienced greater than 1 year of benefit from her last injection. The possibility of spontaneous remission of the tic must be considered in this instance, and the possibility that there was a cumulative effect on either the premonitory sensation or tic musculature.

The cases described in this report demonstrate the advantages of BTX in the management of vocal tics. Both of the patients presented here had refractory vocal tics that were not effectively controlled with

systemic medications. The side effects of the medications prescribed for tics were undesirable, causing their own negative impact on quality of life that perhaps rivaled the tics themselves. With BTX injections, the vocal tics have been well managed and both of the subjects have been able to reduce the need for systemic therapy, thereby contributing to an improvement in quality of life and their ability to return to more natural professional, academic, and interpersonal endeavors. It is asserted that BTX should be considered earlier in the overall management of patients with refractory laryngeal tic symptoms.

REFERENCES