Differential Botulinum Toxin Dosage for Spasmodic Dysphonia Treatment in Men and Women

Karuna Dewan,1 MD; C. Richard Stasney,2 MD; Apurva Thekdi,2 MD
1Bobby R. Alford Department of Otolaryngology- Head and Neck Surgery, Houston, TX, 2Texas Voice Center, Houston, TX

ABSTRACT

Spasmodic dysphonia is a voice disorder resulting from disrupted laryngeal motor control causing involuntary spasms of the laryngeal musculature during phonation. These involuntary movements may cause the vocal folds to inappropriately hyper- or abduct. As a type of dysphonia, spasmodic dysphonia is characterized as a chronic neurologic disorder of central motor processing causing action-induced muscle spasms. The average age at onset of spasmodic dysphonia is approximately 40 years, occurring more frequently in women.5

Chemodenervation of the affected muscle is the standard of care for spasmodic dysphonia treatment. Controversy remains concerning adequate initial and maintenance dosages of this toxic medication. The objective of this study is to identify a differential response to botulinum toxin between male and female spasmodic dysphonia patients.

Study Design: Retrospective chart review; Level of Evidence: 2a

Methods: Patients presenting with symptoms consistent with a diagnosis of spasmodic dysphonia (strained-strangled voice, choked voice, frequent glottic stops) were treated with injection of botulinum toxin according to standard clinical practice.

Results: 127 patients were treated with botulinum toxin injection for spasmodic dysphonia over a 15-year period. There was no significant difference in final botulinum toxin dosage used at the time of initial injection. There was however significant difference in final botulinum toxin dosage between men and women (P=0.04) treated with more than one injection. There was no significant difference between the men and women, in terms of age, subtype of spasmodic dysphonia, and injection location. There was a significant difference between male and female patients with respect to change of dosage during the treatment interval. Female patients demonstrated a greater change in dosage over time as compared to their male counterparts (P<0.00).

Conclusions: Over time female spasmodic dysphonia patients require increasing dosages of botulinum toxin treatment. This likely represents dose optimization rather than changing responses to botulinum toxin over time. Based on the results of this data analysis, we recommend a lower initial dosage of botulinum toxin in men.

INTRODUCTION

Spasmodic dysphonia is a voice disorder resulting from disrupted laryngeal motor control causing involuntary spasms of the laryngeal musculature during phonation. These involuntary movements may cause the vocal folds to inappropriately hyper-adduct or abduct. As a type of dysphonia, spasmodic dysphonia is characterized as a chronic neurologic disorder of central motor processing causing action-induced muscle spasms. The average age at onset of spasmodic dysphonia is approximately 40 years, occurring more frequently in women.5

Chemodenervation of the affected muscle is the standard of care for spasmodic dysphonia. Botulinum toxin is the primary pharmacological treatment for this condition inhibiting the release of acetylcholine at the motor end plate. The result is a temporary paresis or paralysis of the injected muscle. Botulinum toxin is administered either unilaterally or bilaterally. Treatment with botulinum toxin leads to a typical three-part cycle with an initial breathy phase characterized by some voice improvement. The middle phase consists of the peak improvement in voice quality and the final phase is a gradual decline.6

Manipulation of the airway involving botulinum injection of the vocal cord muscle, necessitates the delineation of guidelines for dosage and administrative technique. At present few dosage guidelines exist for achieving satisfactory vocal function. In this study we hope to provide some insight into the differential dosage required for treatment of spasmodic dysphonia in male and female patients.

METHODS AND MATERIALS

Between August 1992 and August 2009, 127 men and women underwent at least one botulinum toxin injection for treatment of spasmodic dysphonia. 112 of these patients underwent at least 2 treatments with botulinum toxin during the 17 year study period.

Patients underwent injection of botulinum toxin into one of three sites based upon their diagnosis. The three locations include the thyroarytenoid muscle, the false vocal fold and the posterior cricoarytenoid. Two different injection methods were used. One author (CRS) performed injection via the cricothyroid membrane using direct visualization with a flexible fiberoptic laryngoscope. Another author (AAT) injected using EMG guidance, also via the cricothyroid membrane. The PCA muscle was injected by rotating the larynx medially and approaching the muscle from behind. A 25 gauge Teflon coated needle was used in both cases and remained submucosal at all times. The groups examined were compared using a Wilcoxon-signed-rank test.

One hundred twenty-seven patients underwent at least one injection of botulinum toxin to treat spasmodic dysphonia. One hundred twelve of these patients underwent at least two injections. The study cohort was 66.8% female. There was no significant difference in the proportion of patients with adductor spasmodic dysphonia between men and women. Patients diagnosed with adductor spasmodic dysphonia were injected in the thyroarytenoid muscle or in the false vocal folds. Patients with abductor spasmodic dysphonia were injected in the posterior cricoarytenoid. There was no significant difference between men and women with respect to the site of injection. In patients receiving unilateral injections, the side of injection was evenly split with 56.1% of men and 46.5% of women receiving a right-sided injection. There was no significant difference between men and women with the side of injection or between the average initial dose of botulinum toxin used to treat spasmodic dysphonia in males and females. A significant difference was noted in the dosage of botulinum toxin needed to achieve adequate voice outcome in women as compared to men, at the time of final injection. Based upon study results we are able to reject the null hypothesis that no difference exists between botulinum toxin requirements in male and female spasmodic dysphonia patients for adequate voice outcome (P=0.04). For the male patients the average dose of botulinum toxin required to achieve a satisfactory voice outcome decreased by an average of 1.21 units over the treatment period. For women the average dose increased by 1.19 units over the treatment period; a significant difference with Wilcoxon signed rank test (P=0.00). In both the male and female cohorts approximately half of the subjects had a change in the side of injection between the initial and final botulinum toxin treatments.

RESULTS

One hundred twenty-seven patients underwent at least one injection of botulinum toxin to treat spasmodic dysphonia. One hundred twelve of these patients underwent at least two injections. The study cohort was 66.8% female. There was no significant difference in the proportion of patients with adductor spasmodic dysphonia between men and women. Patients diagnosed with adductor spasmodic dysphonia were injected in the thyroarytenoid muscle or in the false vocal folds. Patients with abductor spasmodic dysphonia were injected in the posterior cricoarytenoid. There was no significant difference between men and women with respect to the site of injection. In patients receiving unilateral injections, the side of injection was evenly split with 56.1% of men and 46.5% of women receiving a right-sided injection. There was no significant difference between men and women with the side of injection or between the average initial dose of botulinum toxin used to treat spasmodic dysphonia in males and females. A significant difference was noted in the dosage of botulinum toxin needed to achieve adequate voice outcome in women as compared to men, at the time of final injection. Based upon study results we are able to reject the null hypothesis that no difference exists between botulinum toxin requirements in male and female spasmodic dysphonia patients for adequate voice outcome (P=0.04). For the male patients the average dose of botulinum toxin required to achieve a satisfactory voice outcome decreased by an average of 1.21 units over the treatment period. For women the average dose increased by 1.19 units over the treatment period; a significant difference with Wilcoxon signed rank test (P=0.00). In both the male and female cohorts approximately half of the subjects had a change in the side of injection between the initial and final botulinum toxin treatments.

Table 1. Comparison of Botulinum toxin dosages needed to treat spasmodic dysphonia between men and women.

<table>
<thead>
<tr>
<th></th>
<th>Men</th>
<th>Women</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>N with at least 1 injection</td>
<td>41</td>
<td>85</td>
<td></td>
</tr>
<tr>
<td>Adductor Spasmodic Dysphonia</td>
<td>37 (90%)</td>
<td>78 (90%)</td>
<td></td>
</tr>
<tr>
<td>Age at first injection (years)</td>
<td>55.4 ± 12.8</td>
<td>55.2 ± 12.4</td>
<td></td>
</tr>
<tr>
<td>Initial Botox dose (units)</td>
<td>5.9 ± 0.6</td>
<td>5.89 ± 3.7</td>
<td></td>
</tr>
<tr>
<td>N with greater than 1 injection</td>
<td>34 (83%)</td>
<td>78 (90%)</td>
<td></td>
</tr>
<tr>
<td>Age at final injection (years)</td>
<td>59.6 ± 13.6</td>
<td>60.2 ± 12.6</td>
<td></td>
</tr>
<tr>
<td>Final Botox dose (units)</td>
<td>5.3 ± 0.2</td>
<td>7.2 ± 6.4</td>
<td>0.04</td>
</tr>
<tr>
<td>Change in Botox dose (units)</td>
<td>-1.2 ± 0.9</td>
<td>+1.2 ± 4.3</td>
<td>0.00</td>
</tr>
</tbody>
</table>

Figure 1. Botulinum Toxin injection in the thyroarytenoid muscle.

DISCUSSION

Over time female spasmodic dysphonia patients require significantly greater dosages of botulinum toxin in order to achieve satisfactory voice outcomes, whereas requirements are noted to decrease in their male counterparts. This likely represents dose optimization rather than changing responses to botulinum toxin over time. Based on the results of this data analysis, we recommend a lower initial dosage of botulinum toxin in men.

CONCLUSIONS

Over time female spasmodic dysphonia patients require significantly greater dosages of botulinum toxin in order to achieve satisfactory voice outcomes, whereas requirements are noted to decrease in their male counterparts. This likely represents dose optimization rather than changing responses to botulinum toxin over time. Based on the results of this data analysis, we recommend a lower initial dosage of botulinum toxin in men.

REFERENCES