Botulinum Toxin A for Treatment of Sialorrhea in Children

An Effective, Minimally Invasive Approach

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Objectives: To report (1) our experience with botulinum toxin A injections into the salivary glands of pediatric patients with sialorrhea, (2) the clinical outcomes of these interventions, and (3) the associated complication rates.

Design: Retrospective cohort study.

Setting: Urban pediatric hospital and pediatric rehabilitation center.

Patients: Forty-five neurologically impaired children.

Interventions: Patients received botulinum toxin A intrasalivary injections between January 2004 and May 2008 at the Hospital for Sick Children in Toronto, Ontario, Canada. All patients received sedation or general anesthesia for their botulinum toxin A injections, which were performed using ultrasonographic guidance.

Main Outcome Measures: Posttreatment assessments included the duration of effect, patient complications, saliva consistency, caregiver willingness to repeat the treatment, caregiver satisfaction with the treatment, and caregiver overall assessment of the child’s posttreatment quality of life.

Results: Forty-five subjects received a total of 91 botulinum toxin A treatments. The mean (SD) duration of effect was 4.6 (5.2) months. Duration of effect (log transformed) was significantly negatively associated with saliva quantity ($P=0.02$), and there was a positive association with both increasing age and female sex, although neither reached statistical significance ($P=0.08$ for each). Seven of the 24 documented complications were major, according to the Society of Interventional Radiology Classification System for Complications by Outcome scale. Thirty-six of the caregivers reported that this treatment improved the child’s quality of life (80%).

Conclusion: Ultrasonographically guided botulinum toxin A injections into the salivary glands are safe and efficacious in the management of sialorrhea in children with neurologic disorders.

SIALORRHEA IS DEFINED AS THE involuntary, passive pooling and spillage of saliva from the mouth due to the inability to process oral secretions. Although it is common in children who have not developed oral neuromuscular control (younger than 24 months), drooling in individuals 4 years or older is considered abnormal. Patients with neurologic disorders such as Bell palsy, mental retardation, and cerebral palsy often experience excessive drooling. In children diagnosed as having cerebral palsy, it is estimated that 10% to 37% have sialorrhea. Saliva is produced by 3 major paired salivary glands (submandibular, parotid, and sublingual) working in conjunction with several hundred minor salivary glands located in the mucosa of the upper aerodigestive tract. On average, an individual will produce 750 mL of saliva per day, with approximately 90% produced by the submandibular and parotid glands. The secretion of saliva is primarily mediated by the parasympathetic nervous system as postganglionic fibers directly innervate the salivary glands. Acetylcholine is the neurotransmitter linking the nerve terminal to the salivary glands. Blocking the cholinergic stimulation of these glands has been demonstrated to decrease salivary production. Botulinum toxin A (BTX-A) has emerged as one of the primary interventional tools...
used in the treatment of sialorrhea. Its application for treating excessive drooling was first reported by Bushara in 1997, who administered BTX-A into the salivary glands of adults with amyotrophic lateral sclerosis. Since this initial report, BTX-A has been applied to a variety of patient populations (from pediatric to geriatric) with various neurologic disorders that cause sialorrhea. Botulinum toxin A inhibits the release of acetylcholine at the nerve terminal by inactivation of the 25-kDa synaptosome-associated protein SNAP-25, a protein essential for the fusion and release of acetylcholine-containing vesicles at the cell membrane. Acetylcholine production and storage is not affected by BTX-A, and a gradual reinnervation of the salivary glands occurs as SNAP-25 is regenerated.

Profuse sialorrhea is physically and psychologically problematic for affected children and their caregivers. Studies have shown that poor saliva management can have a negative impact on a child's psychosocial development, resulting in low self-esteem, anxiety, embarrassment, limited physical contact with family and friends, and social and emotional isolation. Physical concerns that stem from excessive drooling include constant changing of clothes and/or the need to use bibs, difficulty studying and/or completing homework, skin irritation, dental caries, impaired masticatory function, speech impediment, increased susceptibility to periornal infections, loss of electrolytes and proteins, and aspiration pneumonia. Overall, sialorrhea results in a substantial deterioration in the patient's quality of life.

Recent reports of death and major complications (eg, aspiration pneumonia) following the use of BTX-A in neurologically impaired children have been issued by the United States Food and Drug Administration and Health Canada. These reports prompted us to review our experience with BTX-A in the management of sialorrhea. The objectives of this retrospective study are to report our experience with ultrasonographically guided (USG) intrasalivary BTX-A injections in children with sialorrhea, the clinical outcomes of these interventions, and the associated complication rates.

METHODS

PARTICIPANTS

This study is a retrospective medical chart review of all neurologically impaired children who received intrasalivary gland BTX-A (Botox; Allergan Inc, Markham, Ontario, Canada) injections from January 2004 to May 2008. The patient population included new clients and those for whom previous surgical treatment had failed. No patients were excluded from the review, and none of the patients received concurrent medical therapy for the sialorrhea.

The patients were assessed prior to the procedure at a multidisciplinary saliva management clinic at Bloorview Kids Rehabilitation Centre (Toronto). The multidisciplinary team included representatives from otolaryngology, dentistry, speech-language pathology, and social work services. The BTX-A injections were administered at the Hospital for Sick Children (Toronto), and posttreatment assessments were conducted at Bloorview Kids Rehabilitation Centre. The research ethics board at both institutions approved this study, and informed consent was waived.

INJECTION METHOD

All intrasalivary USG BTX-A injections were administered by a pediatric interventional radiologist using a sterile technique. Prior to receiving their BTX-A injections, all patients were sedated or anesthetized by an anesthesiologist. The BTX-A (100 U/vial diluted with normal saline without preservative) was administered percutaneously into the salivary gland using a 25G or 27G needle at a standard dose of 5 U/kg. All doses were divided equally among the glands, with a small volume of 0.25 to 0.30 mL/gland injected into the substance or center of the gland. Usually, both parotid and submandibular glands were injected under real-time USG visualization, unless the gland was absent due to prior surgery or atrophy. Patients recovered in a postanesthetic care unit and were discharged after a 2-hour observation period. Caregivers were contacted by telephone within 48 hours after injection to assess the patient’s condition and identify any early-onset complications. Treatment outcomes were also documented during an outpatient clinic visit.

OUTCOME MEASURES

Duration of effect was defined as the period during which the caregiver subjectively noticed a decrease in the amount of saliva spillage. Other outcome measures recorded were saliva consistency, caregiver willingness to repeat the treatment, caregiver satisfaction with the treatment, and caregiver overall assessment using a visual analog scale of the child’s quality of life after the treatment.

Patient outcomes were assessed via telephone and during an outpatient clinic visit. Any symptom or problem reported by the patient’s caregiver(s) was labeled as a “complication,” which might have resulted in some overstatement. Early-onset complications were defined as problems that developed within the first 48 hours after injection. In contrast, late-onset complications were identified as any adverse effects reported after this period. Each complication was graded using the Society for Interventional Radiology (SIR) Classification System for Complications by Outcome scale. On this scale, the grade reflects the level of medical treatment required to manage the complication. Minor complications that require no therapy and have no consequence are graded “A.” Minor complications that need nominal therapy, have no consequence, but involve an overnight admission for observation only are classified as “B.” Major complications that require therapy and minor hospitalization (<48 hours) are graded “C.” Complications that require major therapy, trigger an unplanned increase in the level of care, and involve prolonged hospitalization (>48 hours) are scored “D.” Those that lead to permanent adverse sequelae are classified “E.” Any complications that result in death are graded “F.”

STATISTICAL ANALYSIS

Data were analyzed using SPSS for Windows statistical software package, version 14.0 (SPSS Inc, Chicago, Illinois). Given that this was a retrospective study, there was no sample size calculation performed. Rather, all available data from patients who received BTX-A injections for sialorrhea management and completed posttreatment assessments were included in the final analysis. Data presented herein are descriptive (eg, observed procedural outcomes, safety, efficacy) and analytical (eg, hypothesis-generation regression models). Both linear and logistic univariate regression models were generated, depending on the response variable. For linear regression analysis, any
PATIENT CHARACTERISTICS

Between January 2004 and May 2008, 48 patients were treated for sialorrhea with USG intrasalivary gland BTX-A injections. Three subjects were excluded from the study: 2 of these patients died from causes unrelated to BTX-A treatment, and the other was lost to follow-up. Overall, data from 45 patients were included in the final analysis. The mean (SD) durations of effect stratified by the main demographic and clinical characteristics of the patients are summarized in Table 1. The mean (SD) age of the subjects was 10.5 (4.1) years, and the mean (SD) weight was 33.8 (20.5) kg. There were a total of 91 intrasalivary BTX-A treatments performed over the course of 4 years, and those patients who had more than 1 treatment were more likely to have undergone previous surgery \( (P = .05) \).

SIALORRHEA OUTCOME

The mean (SD) dose of BTX-A was 117.8 (46.6) U (range, 40-300 U). The mean duration of effect was 4.6 (5.2) months (range, 1-24 months). Univariate linear regression analyses revealed that there was no significant association between the duration of effect (log transformed) and the variables age, weight, sex, number of treatments, or dose (\( P > .05 \) for all). However, despite lack of statistical significance, the log duration of effect increased with age (\( P = .08; \ R^2 = 6.9\% \)) and tended to be higher in girls \( (P = .08; \ R^2 = 7.2\% \)). There was no difference in the duration of effect between patients who had previous surgery and those who did not \( (P = .17) \). More than half of the 45 patients (24 of 45) followed up with additional BTX-A treatment. However, owing to the time sensitivity of the study data (2004–2008), the remaining patients’ follow-up information could not be included for further analysis. Regarding saliva consistency, 21 caregivers reported thicker saliva after the injection (47%) and 3 reported both thick and foamy saliva (7%).

COMPLICATIONS

A total of 24 complications were reported in 15 of the 45 patients. Seventeen of these complications were minor (SIR grade of A or B), while the remaining 7 were major (SIR grade of C or D). One patient experienced both early- and late-onset complications; 3 patients displayed only early-onset complications; and 11 patients reported only late-onset complications (Table 2). Interestingly, girls were 6.3 times more likely to experience late-onset complications than boys \( (P = .01) \), and the occurrence of an adverse event had no significant impact on the duration of effect, the caregiver’s desire to repeat the procedure, caregiver satisfaction, or overall caregiver assessment. No deaths occurred.

CAREGIVER SATISFACTION AND QUALITY OF LIFE

Several variables were significantly associated with caregiver overall satisfaction in univariate logistic regression models. The variables included duration of effect (odds ratio [OR], 24.3) \( (P = .004) \), having more than 1 treatment (OR, 4.8) \( (P = .02) \), and a decrease in saliva output (OR, 9.2) \( (P = .003) \). Thirty-six of the 45 caregivers stated that their experience with USG intrasalivary gland BTX-A injections improved their child’s quality of life (80%); 6 said that there was no improvement (13%); and 3 believed that the child under their care was worse off for having had the treatment (7%). Caregivers who reported willingness to repeat the procedure (OR, 13.9) \( (P = .004) \) and who reported children with decreased saliva output (OR, 24.8) \( (P = .01) \) were also more likely to report an improved effect.

COMMENT

Numerous studies have reported the effect of BTX-A on drooling in children with neurologic conditions...
Most of those studies were prospective; 1 was a randomized controlled trial; 2 were controlled clinical trials; and 2 were case reports. However, because the study designs were highly variable in terms of sample size, site of treatment, and technique used, meaningful conclusions regarding optimal technique and dosing cannot be drawn. Nonetheless, BTX-A in general has been shown to be effective in the management of sialorrhea in children.

To our knowledge, the present study is the largest cohort study of consecutive children treated with BTX-A and observed for a significant amount of time. Moreover, it is one of the few reports to examine patients who underwent repeated injections and previous surgical interventions for sialorrhea. One of the primary outcomes measured was the efficacy of BTX-A treatment for children with sialorrhea. The results demonstrate that most of the patients experienced a decrease in saliva production after treatment (32 of 45). However, 11 of 45 children had no response, and 2 of 45 patients had an increase in saliva production after receiving BTX-A treatment.

Similar to previous findings, most of our patients reported a subjective reduction in the amount of saliva following treatment with BTX-A. The average duration of effect was 4.6 months, slightly longer than the typical 8 to 16 weeks reported in the literature. One possible explanation for the longer duration of effect is the use of the USG technique for targeting the salivary glands. Numerous studies have shown that the use of USG improves the safety and efficacy of this procedure by ensuring the accuracy of the injection.

Within the cohort studied, a longer duration of effect was observed in girls and older children. It is recognized that female patients are more sensitive to the xerogenic effects of pharmacotherapy and that male patients are more likely to form neutralizing BTX-A antibodies. As far as age is concerned, older patients are more likely to have received other forms of sialorrhea management (eg, oral motor therapy, help with their posture, behavioral feedback, dental work, medication), which, when combined with BTX-A treatment, result in prolonged duration of effect. Interestingly, to our knowledge, no previous BTX-A study has found age to influence the duration of effect in sialorrhea therapy.

Of the 11 patients who displayed no response to the treatment, 7 had previous intrasalivary gland BTX-A injections, and 1 subject had received an intramuscular injection of BTX-A. These patients might have developed BTX-A antibodies, making them resistant to treatment. It is well established that 3% to 10% of patients who receive large doses or repeated injections of BTX-A can develop BTX-A antibodies. An assay to measure BTX-A antibody levels is not available at our institution.

Preexisting neurologic conditions may have also influenced outcome results in those patients who reported a worse response or nonresponse to BTX-A therapy. In individuals with neurologic disorders, sialorrhea is often the result of poor head control, dental malocclusion, poor oral motor control, and/or a decreased frequency of swallowing. Disorders that cause dysphagia via inflammation or mechanical obstruction of the esophagus (achalasia, stricture, and gastroesophageal reflux) also increase the likelihood of developing sialorrhea.

One-third of our patient cohort experienced at least 1 early or late problem, which, erring on the side of overcall, we labeled a complication. Similar complications were reported in previous studies where BTX-A was used to treat sialorrhea. The most serious compli-

### Table 2. Complications Experienced by Patients

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Treatments, No.</th>
<th>Complication</th>
<th>Occurrences, No.</th>
<th>Onset of Complications</th>
<th>SIR Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>Postanesthetic nausea</td>
<td>1</td>
<td>Early</td>
<td>B</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>Vomiting</td>
<td>1</td>
<td>Late</td>
<td>B</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>Loss of voice</td>
<td>1</td>
<td>Early</td>
<td>A</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td>Aspiration pneumonia</td>
<td>3</td>
<td>Late</td>
<td>D</td>
</tr>
<tr>
<td>5</td>
<td>1</td>
<td>Dry mouth</td>
<td>1</td>
<td>Early</td>
<td>A</td>
</tr>
<tr>
<td>6</td>
<td>2</td>
<td>Speech impairment</td>
<td>1</td>
<td>Late</td>
<td>A</td>
</tr>
<tr>
<td>7</td>
<td>3</td>
<td>Pain</td>
<td>1</td>
<td>Late</td>
<td>A</td>
</tr>
<tr>
<td>8</td>
<td>1</td>
<td>Increased drooling</td>
<td>1</td>
<td>Late</td>
<td>A</td>
</tr>
<tr>
<td>9</td>
<td>1</td>
<td>Complication due to general anesthesia</td>
<td>1</td>
<td>Late</td>
<td>B</td>
</tr>
<tr>
<td>10</td>
<td>1</td>
<td>Head banging</td>
<td>1</td>
<td>Late</td>
<td>B</td>
</tr>
<tr>
<td>11</td>
<td>2</td>
<td>Vomiting</td>
<td>1</td>
<td>Late</td>
<td>B</td>
</tr>
<tr>
<td>12</td>
<td>1</td>
<td>Difficulty swallowing</td>
<td>1</td>
<td>Late</td>
<td>D</td>
</tr>
<tr>
<td>13</td>
<td>2</td>
<td>Dry mouth</td>
<td>1</td>
<td>Late</td>
<td>A</td>
</tr>
<tr>
<td>14</td>
<td>2</td>
<td>Difficulty swallowing</td>
<td>1</td>
<td>Late</td>
<td>D</td>
</tr>
<tr>
<td>15</td>
<td>1</td>
<td>Speech impairment</td>
<td>1</td>
<td>Late</td>
<td>A</td>
</tr>
</tbody>
</table>

Abbreviation: SIR, Society for Interventional Radiology Classification System for Complications by Outcome scale.

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(Table 3) Most of those studies were prospective; 1 was a randomized controlled trial; 2 were controlled clinical trials; and 2 were case reports. However, because the study designs were highly variable in terms of sample size, site of treatment, and technique used, meaningful conclusions regarding optimal technique and dosing cannot be drawn. Nonetheless, BTX-A in general has been shown to be effective in the management of sialorrhea in children.

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Within the cohort studied, a longer duration of effect was observed in girls and older children. It is recognized that female patients are more sensitive to the xerogenic effects of pharmacotherapy and that male patients are more likely to form neutralizing BTX-A antibodies. As far as age is concerned, older patients are more likely to have received other forms of sialorrhea management (eg, oral motor therapy, help with their posture, behavioral feedback, dental work, medication), which, when combined with BTX-A treatment, result in prolonged duration of effect. Interestingly, to our knowledge, no previous BTX-A study has found age to influence the duration of effect in sialorrhea therapy.

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Preexisting neurologic conditions may have also influenced outcome results in those patients who reported a worse response or nonresponse to BTX-A therapy. In individuals with neurologic disorders, sialorrhea is often the result of poor head control, dental malocclusion, poor oral motor control, and/or a decreased frequency of swallowing. Disorders that cause dysphagia via inflammation or mechanical obstruction of the esophagus (achalasia, stricture, and gastroesophageal reflux) also increase the likelihood of developing sialorrhea.

One-third of our patient cohort experienced at least 1 early or late problem, which, erring on the side of overcall, we labeled a complication. Similar complications were reported in previous studies where BTX-A was used to treat sialorrhea. The most serious compli-
cific questions relating to patient selection, potential sex domized controlled trials are required to address spe-

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submandibular glands for the management of sialor-

intrasalivary gland BTX-A injections in the parotid and

questionnaires to measure outcomes.

statement of complications, and the use of subjective

conclusions must be tempered by the study limita-

important factors such as improved feeding, sleeping,
treatment (80%), as this measure takes into account

improvement in the child’s quality of life after the

were not satisfied (38%); and 1 was unsure (2%). In

had a resolution of symptoms within a few days to weeks.

occurrence of a complication had no

ministered. The remaining complications were tran-
sient, with no long-term sequelae or catastrophic out-

in fact, all patients with a reported complication

had a resolution of symptoms within a few days to weeks.

Interestingly, the occurrence of a complication had no

significant impact on caregiver desire to repeat the pro-
cure and/or caregiver satisfaction. Indeed, the success-

ful management of sialorrhea was more important to the
caregivers than the development of a minor or transient

complication.

To examine caregiver satisfaction and overall

assessment, a posttreatment questionnaire was admin-

istered. Twenty-seven of the 45 caregivers were satis-

ified with the results of BTX-A treatment (60%); 17

were not satisfied (38%); and 1 was unsure (2%). In

contrast, 36 caregivers stated that there was an overall

improvement in the child’s quality of life after the

treatment (80%), as this measure takes into account

important factors such as improved feeding, sleeping,
skin irritation, and social acceptance. Nonetheless, the

conclusions must be tempered by the study limita-
tions, which include retrospective data, possible over-

statement of complications, and the use of subjective

questionnaires to measure outcomes.

In conclusion, our findings support the use of USG
intrasalivary gland BTX-A injections in the parotid and

submandibular glands for the management of sialor-

rhea in children with neurologic disorders. However, ran-
mized controlled trials are required to address spe-
cific questions relating to patient selection, potential sex

and age biases, the optimal injection technique and dose,
and risks of BTX-A treatment. Ongoing research will help
define standardized treatment protocols to further im-
prove the quality of life of affected children.

Submitted for Publication: June 28, 2010; final revi-

sion received October 13, 2010; accepted November 6,

2010.

Published Online: January 17, 2011. doi:10.1001/

archoto.2010.240

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the data in the study and takes responsibility for the

integrity of the data and the accuracy of the data analy-

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ral, and Connolly. Acquisition of data: W. U. Khan,
Campisi, Naderajah, Semenuk, McCann, Roske, McConney-Ellis, Joseph, and Parra. Analysis and interpre-
tation of data: W. U. Khan, Campisi, Shakur, N. Khan,
Parra, Amaral, John, Temple, and Connolly. Drafting of
the manuscript: W. U. Khan, Campisi, Naderajah, Shakur,
N. Khan, and Connolly. Critical revision of the manu-
script for important intellectual content: W. U. Khan,
Campisi, Shakur, Semenuk, McCann, Roske, McConney-Ellis, Joseph, and Parra. Administrative, technical, and material support: W. U. Khan, Campisi, Naderajah, McCann, Roske, McConney-Ellis, Joseph, and Connolly. Study supervision: Campisi and

Table 3. Pediatric Studies Examining the Treatment of Sialorrhea With BTX-A

<table>
<thead>
<tr>
<th>Source</th>
<th>Design</th>
<th>Patients, No.</th>
<th>Affected Glands</th>
<th>Dose</th>
<th>USG</th>
<th>Follow-up</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current study</td>
<td>Retrospective</td>
<td>45</td>
<td>Parotid (n=11) vs parotid and submandibular (n=34)</td>
<td>&lt;5 U/kg</td>
<td>Yes</td>
<td>&gt;24 mo</td>
<td>36 of 45 success</td>
</tr>
<tr>
<td>Alrefai et al, 2009</td>
<td>Controlled clinical trial</td>
<td>24</td>
<td>Parotid (n=11) vs placebo (n=13)</td>
<td>100-140 U</td>
<td>No</td>
<td>1 mo</td>
<td>5 of 9 success</td>
</tr>
<tr>
<td>Reid et al, 2008</td>
<td>Randomized controlled trial</td>
<td>48</td>
<td>All 4 glands (n=24) vs no treatment (n=24)</td>
<td>25 U per gland</td>
<td>Yes</td>
<td>1 y</td>
<td>16 of 24 success</td>
</tr>
<tr>
<td>Gerlinger et al, 2007</td>
<td>Prospective</td>
<td>21</td>
<td>All 4 glands</td>
<td>30-50 U</td>
<td>Yes</td>
<td>Up to 5 y</td>
<td>20 of 21 success</td>
</tr>
<tr>
<td>Banerjee et al, 2006</td>
<td>Prospective</td>
<td>20</td>
<td>All 4 glands</td>
<td>2 U/kg</td>
<td>Yes</td>
<td>12 wk</td>
<td>89% success</td>
</tr>
<tr>
<td>Kim et al, 2006</td>
<td>Case report</td>
<td>2</td>
<td>Submandibular and single-event multilevel chemoneurolysis</td>
<td>1 U/kg per gland</td>
<td>Yes</td>
<td>5 mo</td>
<td>All improved</td>
</tr>
<tr>
<td>Hassin-Baer et al, 2005</td>
<td>Prospective</td>
<td>9</td>
<td>Parotid</td>
<td>10-25 U</td>
<td>Yes</td>
<td>4 mo</td>
<td>3 of 9 improved</td>
</tr>
<tr>
<td>Jongerius et al, 2004</td>
<td>Controlled clinical trial</td>
<td>39</td>
<td>BTX-A (submandibular) vs scopolamine treatment</td>
<td>30-50 U</td>
<td>Yes</td>
<td>6 mo</td>
<td>69% success</td>
</tr>
<tr>
<td>Savarese et al, 2004</td>
<td>Prospective</td>
<td>21</td>
<td>Parotid</td>
<td>15 U per gland</td>
<td>No</td>
<td>6 mo</td>
<td>89% success</td>
</tr>
<tr>
<td>Jongerius et al, 2003</td>
<td>Prospective</td>
<td>44</td>
<td>Submandibular</td>
<td>30-50 U</td>
<td>Yes</td>
<td>6 mo</td>
<td>Feasible</td>
</tr>
<tr>
<td>Suskind and Tilton, 2002</td>
<td>Prospective</td>
<td>22</td>
<td>Submandibular (n=12) and all 4 glands (n=10)</td>
<td>10-40 U per gland</td>
<td>Yes</td>
<td>&gt;2 mo</td>
<td>All improved</td>
</tr>
<tr>
<td>Bothwell et al, 2002</td>
<td>Prospective</td>
<td>9</td>
<td>Parotid</td>
<td>5 U per gland</td>
<td>No</td>
<td>4 mo</td>
<td>55% success</td>
</tr>
<tr>
<td>Jongerius et al, 2001</td>
<td>Case report</td>
<td>3</td>
<td>Submandibular</td>
<td>30-50 U</td>
<td>Yes</td>
<td>4 mo</td>
<td>All improved</td>
</tr>
</tbody>
</table>

Abbreviation: BTX-A, botulinum toxin A; USG, ultrasonographic guidance of injection.

Financial Disclosure: None reported.

REFERENCES