The Role of Botulinum Toxin A in the Establishment of Symmetry in Pediatric Paralysis of the Lower Lip

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Facial paralysis results in variable degrees of functional deficits and aesthetic asymmetry. Severe cases of paralysis often require surgical reconstruction with nerve and muscle transfers, whereas milder cases can be treated with diaphragmatic muscle transfer, sling suspension, or orbicularis advancement, which are not uniformly successful, or managed nonsurgically with physiotherapy and rehabilitation strategies. As an adjunct to physiotherapy, botulinum toxin A, a neurotoxin that prevents the release of acetylcholine, has been used for improvement of facial symmetry. Its purpose is the weakening of strong muscles on the nonparalyzed side of the face.

The use of botulinum toxin A for facial paralysis has been described in adults and more specifically for protective ptosis in the treatment of lagophthalmos after iatrogenic nerve injury and hyperlacrimation. Use of botulinum toxin A in children is very limited, with one report of 11 pediatric patients treated for focal synkinesis after facial paralysis and another report of treatment of lower lip asymmetry that included some pediatric patients. The purpose of this study was to examine the use of botulinum toxin A in children with facial paralysis, focusing on indications, technique, and rate of complications.
Methods

Patient Selection
We obtained approval from the research ethics boards of The Hospital for Sick Children, Toronto, Ontario, Canada, and the Massachusetts Eye and Ear Infirmary (MEEI), Boston. Written informed consent was obtained from the patients or a family member. We performed a retrospective review of health records for all patients with facial paralysis who had been treated with botulinum toxin A in our institutions from January 1, 2004, through December 31, 2012. A multidisciplinary team approach was involved in the treatment of these patients. The team included a plastic surgeon (R.M.Z. and G.H.B.) or an ear-nose-throat surgeon (T.H.), a physiotherapist, and an occupational therapist.

Data Collection
The inclusion criteria consisted of all patients younger than 18 years with facial paralysis who were treated with botulinum toxin A and had a minimum of 2 years of follow-up after the last injection. Data included demographic information, characteristics of facial paralysis, surgical procedures, information pertaining to botulinum toxin A injections (doses, number of injections, and time intervals), and reported complications.

Injection Technique
Injection of botulinum toxin A was performed under deep sedation or general anesthesia in patients younger than 10 years and with no anesthesia for older patients. Injection sites were marked before administration of anesthesia, at locations best correlating with muscles causing the greatest degree of asymmetry. Depressor or levator muscles of the lip were injected at the points causing maximum depression or elevation of the lip. For treatment of focal synkinesis, injection points were marked over synkinetic muscles at areas with the most prominent synkinetic contractions and least risk for functional impairment. Injection sites were prepared with isopropyl alcohol. Doses of botulinum toxin A that were used for each muscle are summarized in Table 1, and injection sites are shown in Figure 1.

Measurement of Facial Symmetry
The facial analysis software developed by the MEEI has been validated for measuring facial symmetry. We used the software to measure the difference in vertical aperture between the paralyzed and nonparalyzed sides of the lip, which was defined as the lip deviation in each photograph. For each patient, outcomes were determined by the change in lip deviation before and after botulinum toxin A injection (Figure 2).

Statistical Analysis
Values of lip deviation before and after botulinum toxin A injections (at rest and while smiling) were compared across evaluations by repeated-measures analysis of variance using commercially available software (PROC-Mixed SAS, version 9.3; SAS Institute Inc). Statistical significance was determined as \( P < .05 \).

Results
We included 18 patients in this study. Demographic patient data are summarized in Table 2. Patients ranged in age from 4 to 17 years (mean [SD] age, 11.2 [4.7] years). The 3 primary indications for treatment were focal lip asymmetry (\( n = 11 \)), extensive hemifacial asymmetry (\( n = 5 \)), and focal synkinesis (\( n = 2 \)). Fourteen patients were female and 4 were male. Five patients had undergone reconstructive surgery for facial paralysis before botulinum toxin A treatment. Two of these patients had been treated with nerve cable grafts after trauma and tumor resection. Both patients had residual hemifacial asymmetry and focal synkinesis and were treated with botulinum toxin A injections to the orbicularis oculi, lip depressors, mentalis, and platysma. Three additional patients had been treated with a gracilis muscle transfer (as a 1-stage procedure with coaptation to the masseteric nerve in 1 patient and as a 2-stage procedure after facial nerve cross-graft in 2 patients). All 3 patients were treated with botulinum toxin A for focal lip asymmetry.

The botulinum toxin A injection data by indication group is summarized in Table 3. The 11 patients treated for focal lip
Asymmetry had a mean of 3.6 botulinum toxin A treatments compared with 8.4 for the 5 patients in the hemifacial group and 7.3 for the 2 patients in the focal synkinesis group. The median time between botulinum toxin A treatments was 4 months. Two of the patients treated for focal lip asymmetry underwent subsequent myectomy. During a minimum of 2 years from the last injection, no patients experienced complications attributed to botulinum toxin A.

We used the MEEI facial analysis software for evaluation of the deviation correction before and after botulinum toxin A injection. The mean (SD) dynamic deviation before the injection was 3.5 (1.7) mm, whereas the mean (SD) dynamic deviation after the injection was 1.5 (0.8) mm. The deviation correction was evaluated at a mean (SD) of 61% (6%) and was statistically significant ($P = .04$).

### Discussion

Asymmetry of the lower lip secondary to facial nerve dysfunction presents with challenging considerations. Several different techniques have been postulated to regain symmetry, including surgical and nonsurgical approaches. A standardized protocol has also been established to provide physicians with management techniques to improve patient satisfaction and to offer physicians and patients insight into the likely outcome. Thus, multiple studies have shown that botulinum toxin A has a well-established objective benefit in

### Table 2. Summary of Patient Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at presentation, mean (SD) [range], y</td>
<td>11.2 (4.7) [4-17]</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>4</td>
</tr>
<tr>
<td>Female</td>
<td>14</td>
</tr>
<tr>
<td>Laterality of paralysis</td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>7</td>
</tr>
<tr>
<td>Left</td>
<td>10</td>
</tr>
<tr>
<td>Bilateral</td>
<td>1</td>
</tr>
<tr>
<td>Cause of paralysis</td>
<td></td>
</tr>
<tr>
<td>Acquired</td>
<td>11</td>
</tr>
<tr>
<td>Congenital</td>
<td>7</td>
</tr>
</tbody>
</table>

*Unless otherwise indicated, data are expressed as number of patients.
the control of facial hyperkinesis in patients with facial nerve disorders. Studies have established the associated quality-of-life benefit and reaffirmed its important role in the multimodality management of facial nerve disorders. Botulinum toxin A is injected to the normal side to weaken it, thus allowing the weaker affected side to overcome the effect of the contralateral normal muscle and provide a more symmetrical smile.

Despite the numerous studies showing a benefit of botulinum toxin A in the adult population, very few studies have considered its role in the pediatric population. Terzis et al.16 studied 11 pediatric patients presenting with focal synkinesis after facial paralysis and compared facial nerve cross-grafting and secondary microcoaptations with direct muscle neurotization with or without botulinum toxin A injection. The authors concluded that facial nerve cross-grafting with botulinum toxin A injection was effective despite having only 2 patients treated in that group and a total of 4 pediatric patients receiving botulinum toxin A treatment.

This study represents the largest pediatric population, to our knowledge, treated with botulinum toxin A. A total of 18 patients were included from The Hospital for Sick Children and the MEEI. Unlike those of previous studies, our patient population included 11 patients treated for focal lip asymmetry, 5 patients with extensive hemifacial asymmetry, and 2 patients with focal synkinesis. Moreover, we used the MEEI facial analysis software, which has been validated for measuring facial symmetry,18 to quantify the difference in vertical aperture between the paralyzed and nonparalyzed sides of the lip and found significant differences before and after botulinum toxin A injections with a 61% correction. We have also shown that botulinum toxin A did not result in any complications during a minimum of 2 years from the last injection.

Furthermore, our patients continued to show symmetrical results in follow-up, which gives insight into a potential mechanism of action and its important role in the pediatric population. As such, some investigators believe that botulinum toxin A, especially when used in conjunction with physiotherapy,20 can promote better permanent symmetry21 through the creation of new motor patterns as a result of central motor learning.22 As such and knowing the potential for plasticity, the introduction of this treatment in the pediatric population can prove to be more beneficial. These patients will require long-term follow-up to determine permanence of the symmetry, which is a limitation of this study.

Conclusions

Botulinum toxin A injection represents an important adjunct therapy in the reestablishment of symmetry in the pediatric patient population with facial paralysis. We have shown that botulinum toxin A significantly improves symmetry of the lower lip, is safe, and has a potential for restoration of permanent symmetry.

### Table 3. Botulinum Toxin A Injection Data by Indication Groups*

<table>
<thead>
<tr>
<th>Patient Characteristic</th>
<th>Indication</th>
<th>Lip Asymmetry (n = 5)</th>
<th>Hemifacial Asymmetry (n = 2)</th>
<th>Focal Synkinesis (n = 2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reanimation procedure before injection, No. of patients</td>
<td></td>
<td>3</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>No. of injections, mean (range)</td>
<td></td>
<td>3.6 (1-8)</td>
<td>8.4 (2-23)</td>
<td>7.3 (3-15)</td>
</tr>
<tr>
<td>Time between injections, median (range), mo</td>
<td></td>
<td>4 (2-15)</td>
<td>4 (3-6)</td>
<td>4 (2-15)</td>
</tr>
<tr>
<td>Subsequent myectomy, No. of patients</td>
<td></td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

* No patients experienced complications attributed to botulinum toxin A.

### References


