Botulinum toxin therapy in congenital esotropia
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Abstract

Background: Botulinum toxin has been used in congenital esotropia as an alternative treatment with the purpose of reducing ocular alterations as well as reducing sensory disturbances. Good results have been observed with treatment. The target is to present results of congenital esotropia in children <6 years old treated with botulinum toxin.

Methods: A retrospective study was performed including patients <6 years old without psychomotor retardation and who were diagnosed with congenital esotropia. All subjects had application of botulinum toxin, completing 1 year of follow-up.

Results: We included 60 patients with an average age of 1.36 and average deviation of 39 prism diopters (PD). Twelve patients had a large deviation (20%), 25 with a medium deviation (42%) and 23 patients had a small deviation. Toxin at a dose of 5, 7.5, or 10 IU was applied, depending on the deviation. After 1 year, 40% (24 children) had <10 PD of deviation. Esotropia was observed in 39 children (65%), 38 with a small residual esotropia and only one patient with a mild residual esotropia. There was a small consecutive exotropia in seven patients (11.7%), and orthoposition in 14 children (23.3%); 17 patients had immediate exotropia >40 DP.

Conclusions: Success of botulinum toxin application was 55% with an average of 1.2 applications. Medium or large consecutive esotropias lasting 6 months after application have guaranteed a better result.

Key words: congenital esotropia, exotropia, orthoposition, botulinum toxin.

Introduction

Congenital esotropia is the type of strabismus most frequently seen in the ophthalmology unit in up to 55% of patients.1,2 It appears between 2 and 4 months of life. Its etiology is unclear and many authors have proposed some theories. A defect of the brain fusion has been described as an origin or a mechanical alteration that triggers loss of ocular alignment. Other environmental factors that have also been associated are prematurity, low birth weight, neonatal hypoxia, smoking, alcohol or drug use by the mother during pregnancy.3-6

For strabismus, several studies have been published in regard to botulinum toxin to demonstrate the advantages and results under different strabologic conditions such as congenital esotropia, residual accommodative esotropia, postoperative deviations, strabismus associated with high myopia, intermittent and constant exotropia, paralytic or paretic strabismus, strabismus in infant aphakia, some special types of strabismus, early stages of thyroid myopathy,7-16 some cases of nystagmus and strabismic patients with multiorgan abnormalities who according to their systemic condition do not have a surgical treatment option. Good results are seen in the majority of the cases depending on the type of patients, predominant clinical picture and according to the author of the series consulted.17-25 For treatment of congenital esotropia, different options have been proposed. Some authors consider early surgery to be important in order to recover binocularity as soon as possible and to treat amblyopia if it exists.26-28

Among these treatment options is botulinum toxin, with satisfactory results being reported depending on the study author. McNeer et al.,8,9 in their study of 76 patients, reported 89% success. Gomez de Liaño et al.29-30 reported 76% success in a study of 107 patients. Hauviller and Gamio,31 in 62 treated patients, reported 64% success. This caused us to consider botulinum toxin to be a good treatment option for patients with congenital esotropia.

The objective of this study was to identify the percentage of success in the Hospital General de Mexico with botulinum toxin in the treatment of congenital esotropia in children <6 years of age.
Subjects and Methods

This was a retrospective, cross-sectional observational study conducted between March 8, 2004 and December 14, 2012 in patients from the General Ophthalmology Hospital in Mexico with a diagnosis of congenital esotropia. A sample was taken from a cohort of patients with diagnosis of congenital esotropia, <6 years of age, without psychomotor retardation, spherical equivalent to less than +4 prism dipters (PD) and with no history of extraocular muscle surgery. Minimum follow-up was 1 year after application of the botulinum toxin.

Clinical files were reviewed of 68 patients diagnosed with congenital esotropia who received an ophthalmic examination and complete strabismus evaluation that included measurement of visual acuity depending on age and patient cooperation using a pattern of fixation to assess vision HOTV primer or using Snellen chart. The refractive state was determined with cycloplegia with atropine (1%), one drop was applied every 12 h for 3 days before the study or cyclopentolate (1%), two drops were separated by 15 min in both eyes 45 min before exploration. The usual technique was followed with halogen retinoscope (3.5 v, Welch Allyn). Strips were used for retinoscope or phoropter and the fundus of the eye was also reviewed. Strabismus examination included alternating and monocular occlusion. Size of the deviation was measured with alternating shielding and prisms in cooperative patients and with the method of Krimsky or Hirshberg on those patients who were unable to assist. Exploration of ductions and determination of the vertical deviation was done.

To determine the amount of botulinum toxin applied in each case, the deviation was classified as small (20-35 PD), medium (36-45 PD) and large (>46 PD). Five units of toxin was indicated in each hamstring for small esotropias, 7.5 U for medium ones and 10 U for large deviations. The amount of toxin applied to each patient was based on extent of the deviation and previously applied doses or whether for the first time. When the result was not optimal with a single dose, a larger dose was applied in the second injection.

Type A botulinum neurotoxin was used. The lyophilisate was diluted in 2 ml of sterile saline solution with no preservatives to obtain a concentration of 5 IU for each 0.1 mL. Botulinum toxin was applied in both hamstrings under sevoflurane sedation at 2% and 100% oxygen. A topical anesthetic of tetracaine was used, which was instilled into the conjunctival sac and with a swab impregnating the area corresponding to the injected muscle. The application was performed with a 27 G needle with transconjunctival muscle as distal as possible from the tendon and with the needle inserted in its entire length, without electromyosonogram. Post-injection revisions were made at 7 days, 3 months, 6 months and 1 year. The second application was indicated for patients with residual deviations of >25 PD.

After the injection, the deviation was re-assessed. Results were considered good if after 1 year from the application of the botulinum toxin no deviation was observed or if the deviation was small (±10 PD). Descriptive statistics of the variables were carried out using the SPSS v.17.00 statistical package for Windows to calculate averages and percentages.

Results

There were 68 patients recruited, of which eight were excluded: one patient who required surgery at 6 months due to esotropia >50 PD and seven patients were excluded due to lack of follow-up. In total, 60 patients were analyzed: 28 females (46.7%) and 32 males (53.3%) with a mean age of 1.36 years (range: 5 months to 5 years); 47 patients were <2 years old and 13 patients were between 2 and 6 years of age.

Prior to the application of the botulinum toxin, 12 patients (20%) had large deviations and received 10 IU, 25 patients (42%) had medium deviations and were injected with 7.5 IU and 23 patients (38%) had small deviations and received 5 IU of the toxin. The average deviation (PD) was 39 PD (minimum 20 and maximum 60).

One week after application of the toxin, 56 patients had consecutive exotropia: in 39 (70%) it was small, 13 (23%) had medium, and in four (7%) they were large. Two patients (3%) had no deflection, and two patients (3%) had small residual esotropia (Figure 1); 53 (88.3%) patients had palpebral ptosis, which was transient in all cases. At the 3-month follow-up, all patients had recovered from the ptosis, 15 (25%) remained with small consecutive exotropia, 16 (26.7%) with orthoposition and residual esotropia in 29 patients: 28 with small (46.6%) and one patient with large (1.6%). Of the total, 29 patients (48%) had deviation <10 PD (Figure 1). At the 6-month follow-up, there were only six patients with small consecutive exotropia (10%). Thirteen patients (21.7%) had orthoposition; 41 patients had residual esotropia: 40 with small (66.6%), one with large (1.6%). Of the total, 23 patients (38%) had a minor deviation (<10 PD) (Figure 1). At the 1-year follow-up, small consecutive exotropia was observed in seven patients (11.7%), orthoposition in 14 (23.3%), esotropia in 39 cases: 38 (63.3%) with small and one patient (1.6%) with medium. Of the total, 24 (40%) had a deviation <10 PD (Figure 1 and Table 1) and of these patients, 20 (83%) were successfully injected before 2 years of age and four patients (17%) after 2 years of age.

In 17 patients (28.3%) with poor results, one required surgery for a large residual esotropia, 16 (27%) required
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Figure 1. Type of deviation and magnitude at 7 days, 3 and 6 months and 1 year after the injection of botulinum toxin.

Figure 2. Relationship between the position after the first week of application of botulinum toxin and results at 1-year follow-up, which shows that the immediate consecutive exotropia is related to a higher percentage of positive end results.

Table 1. Comparison of the number of patients with each type of strabismus according to the magnitude during follow-up after the first injection

<table>
<thead>
<tr>
<th>Deviation</th>
<th>1st week</th>
<th>3 months</th>
<th>6 months</th>
<th>1 year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small esotropia</td>
<td>2</td>
<td>28</td>
<td>40</td>
<td>38</td>
</tr>
<tr>
<td>Medium esotropia</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Large esotropia</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Small exotropia</td>
<td>39</td>
<td>15</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>Medium exotropia</td>
<td>13</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Large exotropia</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Orthoposition</td>
<td>2</td>
<td>16</td>
<td>13</td>
<td>14</td>
</tr>
</tbody>
</table>

Discussion

Several authors have reported good results with the application of botulinum toxin as treatment for congenital esotropia. Gomez de Liano et al.\(^\text{10}\) reported on a group of 107 patients with a mean deviation of 35 PD (±7) with application dose of 7.5 IU to 10 IU, with an average of 1.5 applications reporting a success of 74.32% and with better results and less lower initial deflection. Toledo and Saucedo\(^\text{15}\) conducted a study with 51 patients aged 4 months to 2 years with an average deviation of 45 PD. The authors used doses of 5 IU and 7.5 IU, with an average of 1.2 applications, reporting success in 73.9% (success was measured as a parameter of deviation of <15 PD).

McNeer et al.\(^\text{9}\) reported on a group of 76 patients diagnosed with congenital esotropia without psychomotor retardation, with ages between 4 and 48 months and with an average deviation of 33 PD. Patients received an application of 2.5 U of botulinum toxin. The authors reported 89% success. The success parameter was a deviation of 10 PD or less, with an average of 1.8 applications.

Tengtrisorn et al.\(^\text{32}\) reported on a group of 11 patients diagnosed with congenital esotropia. Their ages were 14 to 40 months and they had an average deviation of 40 PD; 72.7% success was reported, having a success parameter alignment of ±10 PD. In our study the success rate was 55%, with an average of 1.2 applications.

a re-application of botulinum toxin 1½ years after the first dose; of these, 15 (94%) had a median residual esotropia and one (6%) patient had a large one. A dose of 2.5 IU (one case), 5 IU (five cases), 7.5 IU (six cases), and 10 IU (four cases) were applied. At 3 months after reinjection, one patient had consecutive exotropia of 30 PD. Five patients remained with median residual esotropia so surgical treatment was performed in four of them. Ten patients had residual esotropia of ≤10 PD.

Of the 14 patients with orthoposition 1 year after application of botulinum toxin, 13 (92.8%) had been injected before immediately at the time of application of the toxin, 11 had exotropia of <10 DP at the 1-year follow-up (Figure 2).
Patients who initially had consecutive exotropia >40 PD remained with this deviation for <6 months, but with better results than those who suffered from small consecutive exotropia or orthoposition (Figure 2). In addition, a direct relationship was found between age at the time of the injection (<2 years) and the possibility of success.

The authors cited obtained similar results because, on average, 74% of patients had improvement in esotropia. The average application administered was similar. Although the studies were conducted in patients from different populations (English, Thai, Spanish, and Mexican), there were no significant differences.

In the particular case of a study conducted in the Hospital General de México, successful results did not coincide with the studies carried out by McNeer,8,9 Gomez de Liaño,32 Tengtrisorn et al.,10,11,29,30 and Toledo and Saucedo15 because in our research we obtained only 55% efficiency. Studies addressed by the authors and those conducted in this research are very similar in terms of the degree of deviation, dose and rate of application of botulinum toxin A and technical application. Perhaps the difference in the success of the application of the toxin in congenital esotropia in our environment is due to factors such as age at the time of application, magnitude of the esotropia, psychomotor retardation in patients not diagnosed at the time of application of botulinum toxin, accommodative factors not determined at the time of patient selection, patients selected with spherical equivalent <4 PD, and delayed re-application of botulinum toxin because this procedure was performed several months subsequent to the first application.

In conclusion, application of botulinum toxin A in congenital esotropia is a good treatment option because it is a fast and safe procedure in children with very good chances of ultimate success.

References