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Original Article

Efficacy of Botulinum Toxin in Patients with Infantile Esotropia: Long-Term Effects with a Single Injection

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Abstract

Objectives: Botulinum toxin A (BTX) can be used for strabismus in cases of congenital esotropia or large-angle horizontal strabismus in adults, as well as acute paretic strabismus when surgical treatment of the ocular muscles is not yet possible. This study investigated the long-term efficacy of BTX in patients with infantile esotropia (IE).

Methods: A single-center, retrospective study was performed. The patients had esotropia onset before 12 months and aged were ≤24 months. A successful outcome was defined as ocular alignment within 8 to 10 prism diopters (PD) of orthotropia.

Results: A record review identified 6 patients: 2 boys and 4 girls. The mean age was 14.3±5.4 months. The mean follow-up time was 30.5±12.4 months. A BTX injection was effective, achieving results of a change in deviation from 34.2±5.8 PD (range: 25-40 PD) to orthophoria.

Conclusion: BTX injections can be considered as a primary treatment for patients with IE that may have successful long-term results. Further longitudinal studies are required to support this conclusion.

Keywords: Botulinum toxin A, infantile esotropia, strabismus.

Introduction

Infantile esotropia (IE) is defined as large-angle convergent deviation. It has an onset in the first 6 months of life. It is often associated with other motor abnormalities, such as inferior oblique overaction, cross fixation, dissociated vertical deviation (DVD), and latent nystagmus. Usually, patients don't have refractive errors.

The US Food and Drug Administration (FDA) approved the use of botulinum toxin A (BTX) for the treatment of strabismus and other ophthalmic disorders, such as blepharospasm and hemifacial spasm in 1989. It is produced from the anaerobic bacteria Clostridium botulinum. BTX inhibits muscle spindles, leading to decreased sensory input and decreased muscle contraction. BTX has not been shown to penetrate the blood–brain barrier in humans. When BTX is injected into the muscle, the peak of the resulting muscle weakness or paralysis occurs in 3 to 5 days and lasts approximately 8 to 12 weeks (1-3).

BTX is frequently used to manage esotropia in children. It may also be used for congenital or acquired esotropia, during surgery for large-angle horizontal strabismus, and in cases of acute paretic strabismus when surgical treatment of the ocular muscle is not yet possible at any age.

This study is a report of the long-term results of a single dose BTX injection and a review of some of the relevant literature.

Methods

This was a retrospective study in conducted by the Strabismus Unit of the University of Health Sciences Beyoglu Eye Training and Research Hospital between January 2014 and December 2017. All of the patients provided written

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Table 1. Demographic characteristics of the patients

Patients	Age (months)	Sex	SD	CM	FH	OT	Preoperative (near) (PD)	Postoperative 1 week (PD)	Postoperative 1 month (PD)	Last visit (PD)	Follow-up (months)
1	24	F	No	No	No	No	25	20 Ti	16 Ti	0	27
2	8	F	No	No	No	No	30	30 Ti	16 Ti	0	16
3	15	M	No	Yes	No	Yes	40	25 Ti	20 Ti	0	30
4	12	F	No	No	No	No	40	30 Ti	20 Ti	0	42
5	12	M	No	No	No	No	35	20 Ti	14 Ti	0	20
6	15	F	No	No	No	No	35	20 Ti	14 Ti	0	48

SD: Standard deviation; CM: Consanguineous marriage; F: female; FH: family history; M: male; OT: occlusion therapy; PD: prism diopters; SD: systemic disease.

informed consent and the study adhered to the Declaration of Helsinki. The study was approved by the review board of our institution.

A diagnosis of IE was the basic inclusion criterion in this study. In this clinic, an average of 111 patients with IE receive BTX injections per year. To be included in the study, the patient had not had a previous BTX injection or strabismus surgery, there must have been a minimum follow-up of 6 months, and the patient received only a single injection.

Refraction values were determined using an autorefracter (Retinomax-K; Righton Opthalmic Instruments, Tokyo, Japan) after administration of cyclopentolate hydrochloride drops (Sikloplejin 1%; Abdi İbrahim İlaç San. ve Tic. A.Ş., Istanbul, Turkey) 2 or 3 times, with a 5-minute interval. The best corrected visual acuity was assessed using the Lea Grating Acuity Test (0.25 CPCM-8.0 CPCM, Licensed by Lea-Test Ltd., Helsinki, Finland). Refraction errors were corrected, and after the correction, near and distance deviation angles were measured with an accommodation target using either the prism cover test or the Krimsky test when the patient complied, and the results were measured and recorded in terms of prism diopters (PD). Eye movement in the 9 cardinal gaze positions was examined, and binocular vision function of communicative patients was assessed using the Titmus and Lang I-II tests. A fundus examination was performed using direct ophthalmoscope.

The patients were examined on the first postoperative day and discharged. Steroid and antibiotic eye drops were used 5 times daily for 5 days. All of the patients received 1 injection and were evaluated at 1 month, 3 months, and 6 months after the injection. Surgical success was considered to be alignment within 8 to 10 PD at distance and near.

Technique of injection

All of the injections were performed under general anesthesia. The conjunctiva was anesthetized with topical anesthesia (Lidocaine 4%). Injection to the muscle was done via the conjunctiva while holding the muscle with forceps. Electromyography was not used. The standard dose in this study was 3 IU (1-6 IU) Botox (Allergan Inc., Dublin, Ireland).

Table 2. Refractive measurements of the patients

Patients	Spherical equivalent	
	Right eye	Left eye
1	+1.50	+1.75
2	+1.75	+2.00
3	+0.75	+1.25
4	-1.25	-0.25
5	+2.00	+1.75
6	+1.50	+1.75

The statistical analysis was performed using SPSS for Windows, Version 14.0 (SPSS Inc., Chicago, IL, USA). Mean (SD) and frequency (percentage) were used to describe the summary data. A paired p t-test was used to determine the mean difference. A p value of <0.05 was accepted as significant.

Results

In all, 2 male and 4 female patients were enrolled in this study. The mean age was 14.3±5.4 months. The mean postoperative follow-up period was 30.5±12.4 months. The DVD and cross fixation have not seen in preoperative evaluation. Two patients had -1/-2 abduction restriction. The demographic characteristics of the patients are provided in Table 1.

The mean spherical equivalent was +1.45±0.86 D in the right eye, +1.40±0.76 D in the left eye (Table 2). The mean preoperative angle of esodeviation was 34.2±5.8 PD (range: 25-40 PD) for near vision, and 28.6±10.6 PD (range: 15-85 PD) for distance (compliant patients).

In the early postoperative period, all of the patients demonstrated exotropia. At the 6-month and final exams, the patients displayed orthotropia. The difference between the preoperative and postoperative values was significant ($p<0.01$). In the final exam, an operation was recommended

for bilateral inferior oblique overaction in 1 female patient.

Discussion

BTX inhibits the muscle, resulting in lengthening and a reduction of the contraction of the antagonist. Patients' sensory mechanisms may also play a role in realignment of the eyes. After the injection, if the patient develops some form of binocular vision, ocular alignment may be maintained throughout life. The development of binocular vision is associated with the patient's age.

Scott (1) was the first to use BTX injections on IE patients. Since then, many studies have reported good effects in strabismus patients and have advocated the use of BTX as an alternative in the treatment of strabismus.

For patients with IE, it is less invasive than muscle surgery, and this treatment is performed under a short anesthetic (3, 4). A BTX injection can be a successful alternative in strabismus management. A Cochrane review found that there was no difference between the use of BTX and surgery in patients requiring retreatment for acquired esotropia or IE. However, BTX injections had poorer results in comparison with surgery in patients who had horizontal strabismus in the absence of binocular vision (2).

According to some reports in the literature, multiple injections are needed for maintained ocular alignment in esotropia patients. De Alba Campomanes et al. (5) injected BTX in 322 children as primary treatment for IE and had a success rate of 45% with a mean number of injections of 1.6 IU. The most important factor for maintaining ocular alignment was the pretreatment magnitude of deviation. In our study, the mean pretreatment magnitude of deviation was 33.8±7.5 PD (range: 25-40 PD) for near vision. This was consistent with the literature. Campos et al. (6) evaluated the results of BTX injections administered to 60 children with essential IE, and the success rate was 88% after a single treatment. The mean age at injection was 6.5 months, in contrast to the age group in our study. Scott et al. (7) suggested that approximately 2.1 injections were required to achieve a 66% success rate. In a prospective report, Gursoy et al. (8) found that after a mean follow-up time of 84 months and an average of 1.4 injections, 68% of the patients had achieved successful alignment.

Early treatment provides a "self-adjusting" sensorimotor mechanism to support stable binocular alignment near orthoposition once the motor system has been suitably modified. In fact, at early ages, the central connections of the sensory and motor visual systems can still be changed (9). McNeer et al. (10) studied a dose of 2.5 IU of Botox in 2 groups of patients formed according to age at the time of injection. Patients who received the BTX injection before 12 months of age had a success rate of 93%, while patients older than 12 months had a success rate of 86%. The mean age was 25 months and 25% required surgery. In our study, only 1 patient was younger than 12 months of age. This can be explained by the fact that our hospital is a not a general hospital.

The BTX dose used in our study was a standard 3 IU. A meta-analysis study showed that the greater the dose of BTX, the lower the success rate; for every 1 IU increase in the mean dose there was a reduction of 0.10% in the success rate (9).

Tejedor et al. (3) suggested that BTX injections are a rapid and less-invasive alternative to reoperation in children who have been unsuccessfully treated with surgery to correct IE. The motor and sensory results obtained were similar. Wan et al. (4) found that BTX was at least as effective as surgery for the treatment of acute-onset comitant esotropia in children. The authors found no significant difference in the success rate between the chemodenervation group and the surgery group.

A major limitation of this study is its retrospective design and the small number of patients. Another limitation is the lack of electromyographic guidance. The rectus muscles were identified without a conjunctival incision, and the injection was performed transconjunctivally with forceps. We did not use a control group in this study because we wanted to present our BTX results.

BTX injections offer several advantages: the effect can be the equivalent of surgical results, it reduces the contracture of paralytic strabismus, and additional surgery can required small angle of deviation.

We achieved long-term success in treating IE with only a single BTX injection. However, further longitudinal studies are required to support these results.

Disclosures

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Conflict of Interest: None declared.

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