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Botulinum Toxin A Treatment of Consecutive Esotropia in Children

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Abstract

Objective—To assess the outcome of Botulinum A toxin (BTXA) to treat surgically overcorrected intermittent exotropia in children.

Methods—A retrospective analysis was performed on a series of children with consecutive esotropia treated with BTXA.

Results—Six children with a mean consecutive esotropia of 21 PD were treated with BTXA at a mean of 19.8 months following strabismus surgery. Two patients underwent a single injection, 3 patients 2 injections, and 1 patient 3 injections. Complications included transient ptosis and a vertical deviation. Mean follow-up from last BTXA injection was 16 months. At last follow-up, 4 of the 6 patients were orthotropic and stereopsis was present in 4 of 5 patients old enough to cooperate with testing. One patient was treated with strabismus surgery following a single BTXA injection.

Conclusions—BTXA is an efficacious treatment for consecutive esotropia in children. However, in our series, two-thirds of patients required multiple injections to achieve the desired outcome and one ultimately had an additional strabismus surgery.

Keywords

Intermittent exotropia; consecutive esotropia; botulinum toxin

Introduction

A consecutive esotropia is a common occurrence following surgical correction of an intermittent exotropia. In fact, many surgeons aim for a small consecutive esotropia since most patients have an exotropic drift in the early postoperative period. Many clinical series have reported better long term alignment after intermittent exotropia surgery in patients with an initial overcorrection., (Raab and Parks 1969; Clarke and Noel 1981; Scott, Keech et al. 1981; Oh and Hwang 2006) However, a recent report by Choi and coworkers (Choi, Kim et al. 2011) failed to confirm this finding after a 4 year follow-up. While a consecutive esotropia resolves spontaneously over time in most patients, a consecutive esotropia may persist in 6–20% of overcorrections. (Burian and Spivey 1965; Fletcher and Silverman 1966; Von Noorden 1969; Hardesty, Boynton et al. 1978) In a child, a persistent consecutive esotropia may result in diplopia and the loss of stereopsis and the development of amblyopia. Dawson et al (Dawson, Marshman et al. 1999) reported that Botulinum Toxin A (BTXA) was an effective treatment for a persistent consecutive esotropia in patients with

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binocular vision. We report the outcomes after BTXA treatment in a series of children with a persistent consecutive esotropia following surgical correction of intermittent exotropia.

Materials and Methods

The study was approved by the Institutional Review Board at Emory University and conformed to the requirements of the United States Health Insurance Portability and Privacy Act. Eligible patients were identified by searching the database of the Emory Clinic for all patients <18 years of age with the diagnosis of esotropia (ICD 378.00) and chemodenervation of extraocular muscle (CPT 67345) between 1994–2010. In addition, a chart review was then performed to identify all children <18 years of age who developed a consecutive esotropia following a unilateral lateral rectus recession/medial rectus resection or bilateral lateral rectus recessions treated with a BOTOX (Allergan Pharmaceuticals, Irvine, CA) injection into one of the medial rectus muscles. Initial surgeries were performed between August 1991 and May 2010 and initial BTXA injections were between July 1994 and June 2010. During this time period, a prismatic correction, strabismus surgery or a BTXA injection was offered as treatment for a symptomatic consecutive esotropia following strabismus surgery for an intermittent exotropia that persisted for 1 month or longer. Patients were excluded if they had any other strabismus surgery other than a unilateral lateral rectus recession/medial rectus resection or bilateral lateral rectus recession, an initial constant exotropia or a follow-up less than 1 month after BTXA treatment. BOTOX was reconstituted with sterile, non-preserved normal saline (0.9% Sodium Chloride) prior to injection. All injections were performed using electromyographic (EMG) guidance. Five patients underwent BTXA injection in the operating room using general anesthesia with a combination of Diprivan (Propofol, APP Pharmaceuticals, Schaumburg, IL) 10mg/mL, Fentanyl 50 mcg/mL (Johnson & Johnson, New Brunswick, NJ) and Ultane (Sevoflurane, Abbott Laboratories, Abbott Park, IL). The BTXA injection in the medial rectus muscle was given immediately after general anesthesia was administered. The EMG signal was usually difficult to hear and in some cases localization of the BTXA injection was based on anatomical landmarks rather than the EMG signal. One patient underwent the BTXA injection in an outpatient clinic using conscious sedation with Midazolam (Versed, Roche Laboratories, Nutley, NJ) and topical anesthesia with 0.5% Proparacaine Hydrochloride Ophthalmic solution (Bausch & Lomb, Tampa, FL). All injections were administered by one of the authors (SRL) into one of the medial rectus muscles. The dose of BTXA was titrated based on the angle of strabismus prior to the initial injection and the response achieved with the first injection for repeat injections. The dose of BTXA ranged from 1–4 units per injection. The angle of strabismus was quantified using the prism-and-alternate-cover test. Stereopsis was quantified using the TNO test (Lameris, Utrecht, Netherlands). The primary outcome was the ocular alignment at distance and near following treatment with BTXA. The secondary outcomes were stereopsis and complications. Visual acuity was assessed using a Snellen chart in older children and HOTV letters in younger children.

Results

Six children; 4 boys and 2 girls at a mean age of 5.7 years (range, age 3 to 8 years) were treated for a consecutive esotropia a mean of 19.8 months (range, 1 to 53 months) after undergoing strabismus surgery to correct an intermittent exotropia. Four patients initially had bilateral lateral rectus recessions and two patients a unilateral lateral rectus recession/medial rectus resection (Table 1). They had an overall mean consecutive esotropia of 21 PD (range, 10 to 40 PD) at distance and 19.5 PD (range, 10 to 30 PD) at near, at the time of treatment with BTXA. The mean consecutive esotropia in the bilateral lateral rectus recessions group was 25 PD (range, 10 to 40 PD) at distance and 22.5 PD (range, 10 to 30 PD) at near versus 13.5 PD (range, 12 to 15 PD) at both distance and near in the unilateral

lateral rectus recession/medial rectus resection group. Preoperatively, one patient had 400 seconds of arc stereopsis (Table 2); stereopsis was absent or could not be assessed because of the child's age in the other 5 patients. One patient (Patient 2) was treated with a Fresnel prism prior to treatment with BTXA. None of the patients were able to achieve binocular single vision with a head position prior to treatment with BTXA.

Patients were treated with a mean of 2.3 units (range, 1–4 units) for the initial BTXA injection in the medial rectus muscle (Table 3). Two patients underwent a single injection, 3 patient 2 injections, and 1 patient 3 injections (1.8 injections per patient). Five patients underwent BTXA injection in the operating room and one in an outpatient clinic using conscious sedation and topical anesthesia. In all patients who had undergone a medial rectus resection, the previously operated medial rectus muscle was injected with BTXA.

Mean follow-up after last BTXA treatment was 16 months (range, 4 to 48 months). At the last follow-up, 4 of the 6 patients were orthotropic at both distance and near. The other 2 patients had a reduction in their esotropia. However, one of these patients subsequently was treated with strabismus surgery. None of the patients developed a consecutive exotropia. Following BTXA treatment, stereopsis was present in 4 of 5 patients that could cooperate with testing. Complications included transient ptosis (33%) and vertical deviations (33%). There were no scleral perforations or orbital hemorrhages.

Discussion

We report resolution of a consecutive esotropia following surgical overcorrection of intermittent exotropia in 4 of 6 (67%) children following one or more BTXA injections. A mean of 1.8 injections were administered per patient. Stereopsis improved in 4 of the 5 patients that were old enough to cooperate with stereopsis testing. Final visual acuity was either the same or better in all patients.

Long-term ocular alignment is not always achieved in children following surgical correction of intermittent exotropia. (Raab and Parks 1969; Scott, Keech et al. 1981; Dawson, Marshman et al. 1999) (Pineles, Ela-Dalman et al. 2010) Most patients are believed to have an exotropic drift during the early postoperative period. For this reason, many surgeons aim for a small consecutive esotropia in patients with an intermittent exotropia. However, in some patients this initial overcorrection may persist and treatment may be required because of diplopia in adults and some children and the risk of amblyopia and losing binocularity in children. (Pratt-Johnson, Barlow et al. 1977; Dawson, Marshman et al. 1999) If a consecutive esotropia is treated with additional strabismus surgery, there is a risk of converting the consecutive esotropia into an exodeviation. (Jampolsky 1976; Jung and Rah 2007) One of the advantages of treating a consecutive esotropia with an injection of BTXA is the low risk of a recurrence of an exodeviation. It has been postulated that the high success rate associated with an injection of BTXA into the medial rectus muscle may be due to the high concentration of singly innervated muscle fibers in the medial rectus muscle, which are more susceptible to BTXA than multiply innervated muscles. (Dawson, Marshman et al. 1999) Most adult patients can be treated in an office setting with BTXA injections using topical anesthesia, but this is not usually possible in young children. In our study, we performed all but one of the BTXA injections in the operating room using general anesthesia.

Scott et al (Scott, Magoon et al. 1990) reported successful realignment with BTXA treatment in a group of children with a consecutive esotropia following overcorrection of intermittent exotropia. In their series, 13 of 15 patients with consecutive esotropia (87%) had a final alignment of 10 PD or less, and one-third had high grade stereopsis; two patients

ultimately underwent additional surgery. Dawson et al (Dawson, Marshman et al, 1999) treated 60 patients with consecutive esotropia with BTXA injections. They reported the best results in a sub-group of 36 patients with binocular vision that were treated a mean of 22 months after their last strabismus operation. Fifteen of these 36 patients were symptom free after a single injection of BTXA. While 16 of these patients were 16 years of age, they did not report the results in children separately. Biglan et al (Biglan, Burnstine et al. 1989) reported on a large series of patients treated with BTXA injections after extraocular muscle surgery. Eight of these patients had a consecutive esotropia following exotropia surgery. Preoperatively they had a mean deviation of 20.5 PD. After treatment with BTXA injections, the mean deviation was reduced to 3.3 PD after a mean follow-up of 20 months. Three patients were given two or more BTXA injections. Only 1 patient underwent an additional strabismus surgery.

In our series, all but one of our patients achieved a final alignment of 10 PD or less in the distance with BTXA treatment alone. Even a higher percentage of the patients in our series (67%) achieved high grade stereopsis. This may have been because we only waited on average 20 months after the last strabismus operation to proceed to treatment with BTXA. The only patient in our study who was old enough to cooperate with stereopsis testing who did not have high grade stereopsis had a delay of over 4 years from the time the consecutive esotropia developed until being treated with BTXA. The other 4 patients with high grade stereopsis at the last follow-up had intervals ranging from 1 to 35 months between the onset of the consecutive esotropia until it was treated with BTXA. The older ages of these patients at the time of the initial strabismus surgery may have also been a factor in the recovery of their high grade stereopsis. The one patient who only had gross stereopsis underwent strabismus surgery at the age of 1 year. Most children with intermittent exotropia have high grade stereopsis. However, this stereopsis can be lost if a consecutive esotropia develops and persists for an extended period of time, particularly in young children. One of the reasons proposed to delay the surgical correction of exotropia until a child is older is to minimize the chance of the child losing their binocularity in the event of a consecutive esotropia developing. This concern is supported by the one patient in our study who only had gross stereopsis.

The optimal time for treating a child with a consecutive esotropia with BTXA is unclear. We treated one child 1 month after he developed a consecutive esotropia. This child only had a 12 PD consecutive esotropia, so it is possible that with a longer follow-up the esotropia may have resolved spontaneously. Another child was treated 2 months after developing a consecutive esotropia, but the child had a 40 PD consecutive esotropia in the distance and it is unlikely that this large of an esotropia would have resolved spontaneously at this point after exotropia surgery. Some of the patients in our series were initially treated with Fresnel prisms. However, this is not usually satisfactory for a child on a long term basis. While generally the children treated within 12 months of the inception of a consecutive esotropia all had an excellent outcome, the patient with the longest delay between the onset of the consecutive esotropia and treatment (Patient 6, 53 months) also had an excellent outcome after 2 BTXA injections.

Dawson et al (Dawson, Marshman et al. 1999) reported transient ptosis in 31% of the patients in their series treated with a BTXA into the medial rectus muscle primarily using EMG guidance in an outpatient setting. We had a similar incidence in our series (33%) despite the increased difficulty of localizing the myoneural junction using EMG guidance with a patient under general anesthesia. However, our incidence of a transient vertical deviation (33%) was higher than that reported by Dawson et al (16%).

Conclusions

In our series, two-thirds of the children treated with one or more BTXA injections were orthotropic at last follow-up. However, all but two of the patients required multiple injections to achieve the desired outcome and one ultimately had another strabismus surgery.

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References

- Biglan AW, Burnstine RA, et al. Management of strabismus with botulinum A toxin. *Ophthalmology*. 1989; 96(7):935–943. [PubMed: 2771360]
- Burian HM, Spivey BE. The Surgical Management of Exodeviations. *Am J Ophthalmol*. 1965; 59:603–620. [PubMed: 14270998]
- Choi J, Kim SJ, et al. Initial postoperative deviation as a predictor of long-term outcome after surgery for intermittent exotropia. *J AAPOS*. 2011; 15(3):224–229. [PubMed: 21665502]
- Clarke WN, Noel LP. Surgical results in intermittent exotropia. *Can J Ophthalmol*. 1981; 16(2):66–69. [PubMed: 7306871]
- Dawson EL, Marshman WE, et al. Role of botulinum toxin A in surgically overcorrected exotropia. *J AAPOS*. 1999; 3(5):269–271. [PubMed: 10532570]
- Fletcher MC, Silverman SJ. Strabismus. I. A summary of 1,110 consecutive cases. *Am J Ophthalmol*. 1966; 61(1):86–94. [PubMed: 5904382]
- Hardesty HH, Boynton JR, et al. Treatment of intermittent exotropia. *Arch Ophthalmol*. 1978; 96(2): 268–274. [PubMed: 629674]
- Jampolsky A. Surgical correction of overcorrections in strabismus. *Am Orthopt J*. 1976; 26:14–19. [PubMed: 970708]
- Jung SH, Rah SH. The clinical course of consecutive esotropia after surgical correction. *Korean J Ophthalmol*. 2007; 21(4):228–231. [PubMed: 18063888]
- Oh JY, Hwang JM. Survival analysis of 365 patients with exotropia after surgery. *Eye (Lond)*. 2006; 20(11):1268–1272. [PubMed: 16167074]
- Pineles SL, Ela-Dalman N, et al. Long-term results of the surgical management of intermittent exotropia. *J AAPOS*. 2010; 14(4):298–304. [PubMed: 20736121]
- Pratt-Johnson JA, Barlow JM, et al. Early surgery in intermittent exotropia. *Am J Ophthalmol*. 1977; 84(5):689–694. [PubMed: 930997]
- Raab EL, Parks MM. Recession of the lateral recti. Early and late postoperative alignments. *Arch Ophthalmol*. 1969; 82(2):203–208. [PubMed: 5796092]
- Scott AB, Magoon EH, et al. Botulinum treatment of childhood strabismus. *Ophthalmology*. 1990; 97(11):1434–1438. [PubMed: 2255516]
- Scott WE, Keech R, et al. The postoperative results and stability of exodeviations. *Arch Ophthalmol*. 1981; 99(10):1814–1818. [PubMed: 7295133]
- Von Noorden GK. Divergence excess and simulated divergence excess: diagnosis and surgical management. *Doc Ophthalmol*. 1969; 26:719–728. [PubMed: 5359561]

Table 1

Patient demographics & type of initial surgery

Patient No./Gender	Age at Initial Surgery (years)	Type of Initial Surgery
1/M	8	LROU-rec
2/F	6	LROU-rec
3/M	5	R&R
4/M	4	R&R
5/M	2	LROU-rec
6/F	1.5	LROU-rec

LROU-rec, bilateral lateral rectus recession; R&R, unilateral lateral rectus recession/medial rectus resection

Table 2

Stereopsis and visual acuity before and after treatment

Patient No.	Pre-BTXA Stereopsis (S/arc)	Pre-BTXA Visual Acuity OD/OS	Final Stereopsis (S/arc)	Final Visual Acuity OD/OS
1	0	20/30 20/30	60	20/20 20/20
2	400	20/30 20/30	40	20/30 20/30
3	0 7	20/20 20/20	40	20/20 20/20
4	0	20/20 20/20	60	20/20 20/20
5	NA	C,S,UM C,S,M	NA	20/40 20/40
6	0	20/20 20/20	0	20/20 20/20

BTXA, Botulinum Toxin A; S/arc, seconds/arc; C, central; S, steady; M, maintained; UM, unmaintained; NA, not available

Table 3

Ocular alignment & BTXA treatment data

Patient No.	Pre BTXA Alignment (PD) (D/N)	Interval from Initial Strabismus Surgery to Initial BTXA injection (m)	Age at Initial BTXA (y)	Total No. of BTXA injections/Units per Muscle for each injection	Time from Last BTXA to Last Follow-up (m)	Ocular Alignment at Last Follow-up (PD) D/N	Complications	Additional Surgery
1	40/30 ET	2	8	2/2.5 RMR, 2.5 RMR	8	0/0	None	None
2	10/10 ET	12	7	1/1.0 RMR	7	0/0	None	None
3	12/12 ET	1	5	2/2.0 LMR, 2.0 RMR	4	0/0	Transient vertical deviation	None
4	15/15 ET	35	6	3/2.0 LMR, 2.0 RMR, 3.0 LMR	48	10/20 ET	Transient ptosis and vertical deviation	None
5	30/30 ET	16	3	1/2.5 RMR	26	18/20 ET	None	Unilateral MRC & LR adv
6	20/20 ET	53	5	2/4.0 RMR, 1.0 RMR	3	0/0	Transient ptosis	None

ET, esotropia; D, distance; N, near; PD, prism diopters; BTXA, Botulinum Toxin A; m, months; y, years; RMR, right medial rectus; LMR, left medial rectus; MRC, medial rectus recession; LR adv, lateral rectus advancement