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Original Article

Treatment of Infantile Esotropia – Comparison Between Botulinum Toxin A and Bilateral Medial Rectus Recession

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Abstract

Objectives: The objective of the study is to evaluate the examination findings, treatment methods, and follow-up results of children diagnosed with infantile esotropia (IE) and to compare botulinum toxin A (BTA) and bilateral medial rectus (MR) recession surgery.

Methods: We retrospectively reviewed the medical records of patients who were diagnosed with IE. The age of the patient and the angle of deviation were taken into account to determine the treatment. Patients who underwent bilateral MR recession surgery and BTA injection were analyzed and the BTA and surgical groups were compared. Successful correction was defined as orthotropia and a deviation of up to 10 prism diopters (PD) after one surgical procedure or 1–3 botulinum injections.

Results: Two hundred and forty-six patients with esotropia were included in the study. Twelve were followed up with refractive correction only. BTA injection was administered to 110 patients, while 124 patients underwent bilateral MR recession. The age of the patients ranged from three to 39 months. Patients were followed for at least 6 months, with a mean follow-up of 24.3 months in the BTA group and 21.7 months in the surgical group (p=0.23). The mean pre-treatment angle deviation was 38.9 PD in the BTA group and 40.1 PD in the surgical group (p=0.62). The success rate for patients with more than 30 PD of deviation was 72% in the surgical group compared to 36% in the BTA group (p<0.001). No statistically significant difference in success rate was observed in patients with deviations <30 PD (surgery 62%, BTA 55%, p=0.26).

Conclusion: Surgical treatment of IE was more successful than BTA injection in patients with large angle deviations (>30 PD). BTA injection can be considered as an alternative to surgery in cases of small to moderate angle deviations (<30 PD).

Keywords: Amblyopia, botulinum toxin, infantile esotropia, strabismus.

Introduction

Infantile esotropia (IE) is defined as esotropia before the age of 6 months with a large angle (usually 30–60 prism diopters [PD]), mild to moderate hyperopia, latent nystagmus, dissociated vertical deviation (DVD), limited abduction, absent or reduced binocular vision, and in the absence of neurological disorders or other systemic abnormalities (1). Although many theories have been proposed, the true cause of IE is

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still unknown (2). Refractive disorders, sensory disorders, motor abnormalities (muscle insertion abnormalities or peripheral nerve disease), physical trauma, and innervational or mechanical factors have been implicated in esotropia (3). Approximately 2–4% of children suffer from strabismus according to surveillance studies (4,5). Amblyopia and binocular vision loss are reported in 40% of these children (6). The consensus view on achieving optimal best corrected visual acuity and binocular vision is to treat all patients as soon as possible after diagnosis of IE (7). Early diagnosis and treatment of strabismus are therefore of great importance. The main goal in the treatment of strabismus is to achieve eye parallelism and protect binocular vision.

Factors such as comitance, the presence of alternation, accommodation and refraction disorders, and stereopsis must be considered when planning surgical treatment. Bilateral medial rectus (MR) recession, unilateral MR recession with lateral rectus resection, and botulinum toxin A (BTA) injection into the MR are treatment options (8,9). Scott first used BTA in 1980 to treat strabismus by temporarily paralyzing the extraocular muscles (10). BTA can correct the deviation in favor of binocular single vision and provide orthophoria in the eyes. Although the effect of the neurotoxin is temporary, it can permanently correct strabismus with single or repeated injections. It can be used alone or as a surgical augmentation in cases of wide-angle deviation. Its use in IE, especially in small infants and with small angle deviations, may also obviate the need for surgery (11,12).

The aim of this study is to describe the methods used to treat IE patients diagnosed in our clinic, to evaluate our results, and to discuss them with previous literature.

Methods

Patients under 6 years of age diagnosed with IE at the Strabismus Unit of Beyoglu Eye Training and Research Hospital between 2002 and 2015 were included in the study. The study was designed retrospectively and approved by the local Ethics Committee (HRU/21.15.25, 2021). The study adhered to the tenets of the Declaration of Helsinki. Inclusion criteria were parental report of esotropia within the first 6 months of life, absence of limitation, and esotropia not due to trauma or inflammatory disease. Patients with refractive errors of up to +3.00 diopters who were examined at our clinic within 6 months of birth were included. Patients who were treated in other clinics and who had significant refractive accommodative components were excluded from the study. Cases with significant vertical deviation, variable angle esotropia, neurodevelopmental abnormalities, previous ocular surgery, or BTA or other ocular pathologies were also excluded. All patients underwent a complete ophthalmic examination, including cycloplegic refraction, duction, and version tests at the first visit. The angle of deviation was measured using a prism or alternating cover test if the patient was co-operative and recorded as a PD value. Hirschberg or Krimsky tests were performed and recorded if the patient was uncooperative. The presence of vertical deviation, inferior oblique overaction, nystagmus, and dissociated deviation were recorded. The decision to treat was made in cases where there was no improvement in deviation after two visits.

The parents of all patients were informed of the risks and benefits of both treatment options and were advised to opt for surgery or BTA injection. Signed consent forms were obtained. Surgery was planned according to the rules suggested in the previous literature and was performed under general anesthesia in all cases. The clinical measurements were not performed by the same doctor each time, but the treatment modalities were performed by the same surgeon for each patient. Surgery and BTA were performed by four experienced strabismus surgeons (BG, EDA, AI, and OBO). BTA was primarily used in all patients under the age of 2 years and/or with small and moderate angle deviations. Surgery was used as the first intervention in patients over 2 years of age and/or with large angle deviations. Surgery was applied if there was additional muscle pathology (such as IOA and DVD). Bilateral MR recession was performed surgically (13). The amount of MR recession used in the surgical method was between 4 and 5.5 mm depending on the deviation angle. None of the patients underwent three muscle procedures in the same session. BTA (Botox®; Allergan, Irvine, CA, USA) injections were administered under inhalation general anesthesia. The toxin was prepared in 3 IU 0.1 saline and injected into the MR muscles using 27-gauge insulin injectors (14). All patients in the BTA group received the same dose of BTA. If the patient was not orthophoric after the last injection (i.e., esotropia greater than 10 PD), up to two additional injections were given after 1–5 months. Surgery was recommended if the patient was still not orthophoric after three doses.

In addition, surgery was the first option if the patient came from out of town for treatment and was considered to be difficult to follow. Orthophoria (motor success) was assessed after a single surgical procedure or 1–3 BTA injections in the bilateral MR muscles. Cases with residual deviation underwent a second strabismus operation. Second surgery in the surgery group or surgery as primary treatment in the BTA group was considered a treatment failure, regardless of final motor alignment.

Secondary surgical procedure data (number of surgeries, indications, number of muscles operated on, dissociated deviations, and oblique muscle hyperfunctions) were recorded.

Data analysis was performed by independent researchers not involved in the study.

Statistical Analysis

Statistical analysis was performed using IBM SPSS for Windows software version 20 (Chicago, IL). Group means of continuous variables were compared using the t-test, while means of categorical variables were compared using Pearson's x^2 test. Multivariate logistic regression analysis was used to analyze the association between successful motor outcomes and continuous variables. Odds ratios (OR) and 95% confidence intervals were calculated for each possible predictive factor. P<0.05 was considered statistically significant between the two groups.

Results

Two hundred and forty-six patients with IE were included in the study. Twelve patients were followed up with refractive correction only, and in these cases, no further intervention was required. Ten cases had a history of prematurity. There was no statistically significant difference between the groups in terms of gender, history of prematurity, refractive spherical equivalent, or mean follow-up time.

Patients were followed for at least 6 months; the mean follow-up was 24.3 months in the BTA group and 21.7 months in the surgery group (p=0.23). The mean age was 27.4 months in the surgical group and 15.7 months in the BTA group (p<0.001) (Table 1). Patients in the surgical group were on average 12 months older at treatment than those in the BTA group (27 months and 15 months, respectively; p<0.001) and also had a longer time to strabismus (mean difference: 12 months; p<0.001). One hundred and twenty patients were male, and 126 were female (Table 1).

One hundred and ten patients received BTA injections, and 124 underwent surgery. In the BTA group, the angle of deviation was less than 30 PD in 70 of 110 patients (63.7%) and greater than 30 PD in 40 (36.3%) patients. In the surgery group, the angle of deviation was <30 PD in 56 of 124 patients (45.2%) and greater than 30 PD in 68 (54.8%) patients (Table 1).

There was no significant difference between the success rates of surgery and BTA (surgery group 62%, BTA group 55%, p=0.26) in patients with angles of deviation of 30 PD or less.

In patients with more than 30 degrees of deviation, the success rate of surgery was 72% compared to 36% with BTA injection (p<0.001).

Successful motor correction was 69% in the surgical group and 41% in the BTA group (p<0.001).

Fifty seven of the 110 patients in the BTA (48.7%) received a single injection, 50 (40.9%) received two injections, and the remaining three patients (10.2%) received three injections.

Residual esotropia persisted in 37 (30%) patients in the surgical group, and consecutive exotropia was noted in four (3.2%) patients.

Of the patients who received BTA, 44 (44%) underwent surgery for residual esotropia and 23 (20.9%) patients with DVD or inferior oblique hyperfunction measured in the primary gaze underwent surgery. Consecutive exotropia was observed in 9 patients (8.2%) who received BTA. Consecutive exotropia improved after 2 months in the BTA group, while it was <15 PD in the surgical group and no treatment was applied. Ptosis was observed in 9 patients in the BTA group and resolved in 3 weeks.

Age at onset of esotropia, age at first treatment, and duration of esotropia were not associated with successful motor outcomes in either group (p>0.05).

According to multivariate logistic regression analysis, decreased angle of deviation and surgical treatment group were considered predictive of successful motor outcome (p<0.05) (Table 2).

Table 1. Comparison of demographic characteristics of patients, pre-operative, and post-operative findings of surgery and Botox groups

	Surgery (n=124)	Botox (n=110)	p
Age	27. 4 (3–39 months)	15.7 (3–36 months)	<0.001
Gender (female/male)	66/58	60/50	0.63
Follow-up duration	21.7 months	24.3 months	0.23
Patients number ≤30 PD esodeviation	56 (45.2%)	70 (63.7%)	0.12
Patients number > 30 PD esodeviation	68 (54.8%)	40 (36.3%)	0.03
Pre-operative mean deviation (PD)	40.1	38.9	0.62
Motor allignment success (orthotropia ±10 PD)	69%	41%	<0.001
Success rate in ≤30 PD deviation angle	62%	55%	0.26
Success rate in >30 PD deviation angle	72%	36%	<0.001
Residuel esotropia	37	44	0.33
Consecutive exotropia	4	9	0.12

PD: Prism diopter; p<0.05 is statistically significant.

Table 2. Multivariate logistic regression analysis of factors that influence successful motor outcome

	Odds ratio	p	95% Confidence ınterval	
Age at onset of esotropia	1.65	0.124	1.53	1.92
Age at first treatment	0.82	0.212	0.56	0.99
Duration of esotropia	0.92	0.546	0.87	1.43
≤30 PD deviation	2.15	0.024	1.96	2.83
>30 PD deviation	0.99	0.321	0.92	1.06
BTA treatment	0.75	0.612	0.68	1.12
Surgical treatment	2.86	0.035	2.75	3.13

BTA: Botulinum toxin A; PD: Prism diopter; P<0.05 was statistically significant.

Discussion

In our practice, we started to treat amblyopia in patients with fixation preferences, and prevention of amblyopia was not associated with the correction of strabismus. In our study, surgery was more effective than BTA injection in patients with deviations greater than 30 PD. However, surgery and BTA injection showed similar efficacy in patients with low and moderate angles of deviation. Spontaneous resolution also occurred in 12 patients with 25-30 PD. Age at onset of deviation, age at first treatment, and duration of deviation were not relevant in either group with successful motor outcomes.

Shon et al. reported spontaneous resolution in three IE patients with deviations of 25–30 PD who were followed up without correction. However, all of these individuals developed poor stereopsis, DVD, and inferior oblique hyperfunction (IOA) with improvements in esotropia (15). Simonsz and Eijkemans reported spontaneous resolution in a few patients with +4.00 diopter hypermetropia and a low (<25 PD) deviation (16). In our study, twelve patients were followed up with refractive correction alone, and these cases did not require further intervention.

Studies have used BTA alone or in combination with surgery to increase the effect of surgery, but in our study, we used BTA alone. Treatment success rates with BTA in IE are variable (8,14,17,18). BTA injection has been shown to be an effective and reliable treatment, especially in the first 6 months of life. Campos et al. described BTA injection as an effective method of treating patients in the first 7 months of life. They reported an 88% success rate in their patients with IE who were followed for an average of 5.2 years (12). In another study, Hauviller et al. described the efficacy of BTA injection as a primary treatment option as similar to that of surgery and also suggested that BTA injection could represent the primary treatment option due to its less invasive nature. In their study, 72% orthophoria ±10 PD was achieved in IE with a mean deviation of 35 PD (range 20–60 PD) (17). There are no reliable data on the stabilization of deviation during 5–10-year follow-up in patients treated with BTA compared to surgery. Gursoy et al. treated 56 patients aged 24 months and younger with BTA or bilateral MR recession and followed them for at least 2 years. The treatment dose of BTA was 4.0 units for the first injection and 2.5 units for the reinjection. With a maximum of three injections or a single surgical procedure, they defined success as 10 prism diopters of orthotropy at the final examination (18).

In their studies, 77% of bilateral MR recession and 68% of BTA injection were successful, with no statistically significant difference (18). In our study, patients in the surgical group were on average 12 months older than those in the BTA group at the time of treatment and also had a longer time to strabismus. We suggest that BTA injection can be used as a primary method, especially in the early periods and in patients with small and moderate deviations. It has been reported that an average of 1.4 BTA injections were given in the studies (14). In our study, half of the patients received one injection, 10% received three injections, and the rest received two injections.

In our study, according to logistic regression analysis, decreased deviation angle and surgical treatment group were considered predictive of successful motor outcome.

In agreement with our study, de Alba Campomanes et al.(13) in their comparison of BTA injection and surgery for IE described surgery as superior to BTA injection in patients with large angles of deviation. Issaho et al. concluded in their meta-analysis that BTA injection into the MR muscles is a safe and valuable alternative to surgery, especially in patients with moderate deviation.

Yagasaki et al. found that early surgery (before 24 months) reduced the severity of DVD and the need for additional surgery (19). Shin and Paik suggested that surgical treatment before 24 months reduced the incidence and severity of spontaneous DVD in patients with IE, especially those with a large angle of deviation (20). In our study, 20.9% of our

patients in the BTA group underwent surgery for DVD and IOA. The rate of DVD and IOA in the surgical group was 19.5%. Cho et al. reported that IOA and DVD development were more frequent in the post-operative period in patients with fundus torsion under general anesthesia, even if there was no DVD and IOA in the pre-operative examination (21). In our study, we evaluated DVD and IOA with clinical examination, as a limitation of the study, we could not demonstrate fundus torsion.

Arslan et al. found that recovery of binocularity with early surgical intervention and prevention of amblyopia was associated with a lower incidence of DVD (22). Magli et al. found that two horizontal muscle surgeries should be preferred in patients with a small angle of deviation and more than two muscle surgeries in cases with a large angle of deviation (9). In another study, Sturm et al. reported that three horizontal muscle procedures (bilateral MR recession and lateral rectus resection) were associated with high success rates in patients with large deviation angles (23). In our practice, we do not operate on more than two muscles in the first operation. Consecutive exotropia developed in 4 patients in the surgical group and in 9 patients in the BTA group. Consecutive exotropia improved after 2 months in the BTA group, while it was less than 15 PD in the surgical group and no treatment was applied.

One of the main limitations of our study is its retrospective nature. Other limitations are the short follow-up period and the inability to accurately assess stereopsis in the group of small children, so we did not include stereopsis in the statistical analysis. In addition, the statistically significant age difference between the groups is also a limitation.

Conclusion

BTA injection is a potential primary treatment modality and an alternative to surgery in patients with small to moderate angles of deviation. Surgical treatment has been shown to be more successful than BTA injection for large-angle (>30 PD) esotropia. BTA injection may be the primary treatment option in children with low to moderate angle (≤30 PD) deviation because it is less invasive and the anesthetic time is short, but it should be noted that repeated injections may be necessary.

Disclosures

Ethics Committee Approval: Patients under 6 years of age diagnosed with IE at the Strabismus Unit of Beyoglu Eye Training and Research Hospital between 2002 and 2015 were included in the study. The study was designed retrospectively and approved by the local Ethics Committee (HRU/21.15.25, 2021). The study adhered to the tenets of the Declaration of Helsinki.

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