



Original research

# Botulinum toxin injection in the patients with Duane syndrome type 1

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## Abstract

**Purpose:** To evaluate the efficacy of botulinum toxin injection in the patients with type 1 Duane syndrome and identify the predictive factors for success.

**Methods:** Sixteen patients with esotropic type 1 Duane syndrome without history of ocular surgery were selected for this interventional case series. The botulinum toxin was injected in the medial rectus of all patients. Visual acuity, dry refraction, cyclo-refraction, ocular motility, and amount of deviation were measured. Complete success, partial success, and failure were defined as residual deviation/face turn less than 8 prism diopters (PD)/5°, 8–20 PD/5–15°, and equal or greater than 20 PD/15°, respectively.

**Results:** Sixteen cases (6 males) were included in our study. The mean esotropia was  $26.27 \pm 8.35$  (12–40 PD) which was reduced significantly to  $13.5 \pm 12.39$  PD during 6 months follow-up ( $p < 0.001$ ). Face turn was improved significantly from a preoperative mean of  $18.27^\circ$  to:  $0.094^\circ$  at 1 week,  $0.11^\circ$  at 1 month,  $3.31^\circ$  at 3 months, and  $7^\circ$  at 6 months ( $p < 0.001$ ). Complete success was seen in 6 patients (37.5%), partial success in 4 patients (25%), and failure in 6 patients (37.5%). There was a significant relation between the amount of forced duction testing (FDT) and the success rate ( $p: 0.019$ ). No complication was seen during injections.

**Conclusions:** Botulinum toxin could be an alternative treatment in Duane syndrome with appropriate case selection. FDT could be a predictive factor for response to botulinum toxin.

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**Keywords:** Duane syndrome; Botulinum toxin; Esotropia

## Introduction

Duane syndrome is a congenital disorder with ocular motility impairment associated with disorder of innervation.<sup>1</sup> The misinnervations convert ocular motility from a normal pattern to the limited movement with globe retraction and narrowing palpebral fissure.<sup>1</sup> Duane syndrome shows different

severities from mild cases with minor limitations in ocular movements to cases with anomalous head posture and significant deviation in primary position. It may be unilateral or bilateral. In bilateral cases, different types of Duane syndrome may be seen in each eye. Horizontal rectus muscle recession is recognized as the main treatment of this disorder.<sup>2</sup> Surgical indications included deviation in primary position, anomalous head posture, marked globe retraction, and large upshoot and downshoot.<sup>3</sup> The treatment corrects the deviation and anomalous head posture without significant improvement of movement limitations.<sup>4</sup> The surgical goals may be obtained by nonsurgical techniques. Botulinum toxin injection into rectus muscles may be an appropriate management in some of the patients with Duane syndrome.<sup>5–7</sup> This study was performed for evaluation of the efficacy of botulinum toxin injection in

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patients with type 1 Duane syndrome and to identify the predictive factors for success.

## Methods

This interventional case series was performed in Farabi Eye Hospital from February 2009 to November 2009. Institutional Review Board approval was gained, and the tenets of the Declaration of Helsinki were followed. Patients with type 1 Duane syndrome associated with significant eso-deviation (at least 12 prism diopters (PD)) in primary position entered the study. Other types of Duane syndrome and history of ocular surgery were considered as exclusion criteria of our study. Informed consent was obtained from all patients or their parents. Pre-injection examinations included: uncorrected and best corrected visual acuity (UCVA and BCVA), dry refraction, cyclo-refraction, complete slit-lamp examination, ocular motility, and amount of deviation and abnormal face turn. The measurement of deviation and face turn were performed by alternate prism cover test and goniometer, respectively (all were measured by one ophthalmologist [A.A.]). Follow-up visits were done pre-operatively and 1 day, 1 week, 1 month, 3 months, and 6 months after the procedure. The patients were categorized into three groups: complete success (residual deviation less than 8 PD and residual face turn under  $5^\circ$ ), partial success (residual deviation between 8 and 20 PD and residual face turn between  $5^\circ$ – $15^\circ$ ), and failure (no significant improvement in deviation and face turn, residual deviation  $\geq 20$  PD and residual face turn  $\geq 15^\circ$ ).

### Method of procedure

The procedure was performed without Electromyography (EMG) guide<sup>8</sup> and under general or local anesthesia. All procedures were done by one surgeon (A.A.). Phenylephrine 2.5% eye drops were utilized twice with 5-min intervals to facilitate muscle findings and carry out fundoscopy after injection to evaluate possible retinal injury. Then forced duction testing (FDT) in horizontal plane was done, and FDT was graded (Table 1). In the next step, the 3.5 IU of Novotox Ultra™ (35 u/vial, DPS company, China and distributed by donaexperts Inc, Montreal, Canada) was injected by needle with a 27-gauge needle. After taking out the needle, an applicator was placed on it for 30 s. The patients were placed

Table 1  
Grading of forced duction testing.

Grading	Definition
1+	1 It was not normal, and 2 It passed from the midline, and 3 The light reflex was not seen on the cornea.
2+	1 It passed from the midline, but 2 The light reflex was seen on the cornea.
3+	1 It reached the midline, but 2 Did not pass from this line (approximately the light reflex was matched with the center of cornea).
4+	Did not reach the midline.

in a semi-sitting position after the injection. Afterward, in suspected cases of sclera penetration, fundoscopy was performed.

### Statistical analysis

The data were analyzed by SPSS version 14 (SPSS Inc, Chicago, USA). The quantitative data were shown as mean  $\pm$  SD. The data were compared by paired t-test. The difference of success rate based on the grading of FDT, gender, and age was analyzed by Chi square test and ANOVA test, respectively.  $p < 0.05$  was considered statistically significant.

## Results

The patients included 6 males and 10 females with the age range of 1–21 years. Duane syndrome involved the left eye in 11 cases (68.75%), the right eye in 3 cases (18.75%), and both eyes in 2 cases (12.5%). There were 11 patients (68.75%) with amblyopia with the distribution of mild (BCVA 20/25–20/40), moderate (BCVA 20/40–20/100), and severe (BCVA worse than 20/100) in 4, 6, and 1 patients, respectively.

All of our patients had esotropia and face turn in the direction of Duane's eye. The mean esotropia was  $26.27 \pm 8.35$  PD (12–40 PD) which reduced significantly to a mean of  $5.5 \pm 13.01$  PD exotropia at 1 week,  $2.55 \pm 12.00$  PD exotropia at 1 month,  $5.43 \pm 11.74$  PD esotropia at 3 months, and  $13.5 \pm 12.39$  PD esotropia at 6 months after the procedure ( $p < 0.001$  in all follow-up visits). Face turn was improved significantly from a preoperative mean of  $18.27^\circ \pm 7.29^\circ$  to:  $0.094^\circ \pm 2.99^\circ$  at 1 week,  $0.11^\circ \pm 3.54^\circ$  at 1 month,  $3.31^\circ \pm 5.10^\circ$  at 3 months, and  $7^\circ \pm 10.19^\circ$  at 6 months ( $p < 0.001$ ). The face turn was completely corrected in 2 patients after Botulinum toxin injection and remained stable up to 6 months follow-up.

Complete success was seen in 6 patients (37.5%), partial success in 4 patients (25%), and failure in 6 patients (37.5%).

Table 2  
Relation between forced duction test and success rate.

			Success		
			Complete	Partial	Failed
FDT	+1	Count	1	1	
		% within FDT	50	50	
		% within success	16.7	25	
	+2	Count	5	1	
		% within FDT	83.3	16.7	
		% within success	83.3	25	
+3	Count		2	3	
	% within FDT		40	60	
	% within success		50	50	
+4	Count			3	
	% within FDT			100	
	% within success			50	
Total	Count	6	4	6	
	% within FDT	37.5	25	37.5	
	% within success	100	100	100	

FDT: Forced duction test.

Table 3  
Mean primary deviation and face turn in 3 success groups.

	Preinjection value	Responses		
		Complete success	Partial success	Failed response
Esodeviation (PD)	26.27 ± 8.35	18 ± 4.42	33.75 ± 4.78	30.83 ± 5.24
Face turn	18.27 ± 7.29	13.67 ± 3.50	22 ± 6.50	21.17 ± 8.94

PD: prism diopter.

There was significant direct relation between the amount of FDT and success rate ( $p: 0.019$ ) (Table 2). There was no significant relation between success rate and age or sex ( $p: 0.378$  and  $0.169$ , respectively). Table 3 shows mean primary deviation and face turn in 3 success category groups.

No major complication (such as scleral perforation) was seen during the procedure. Subconjunctival hemorrhage (5 patients), ptosis (mild in 5 patients, moderate in 3 patients), and vertical strabismus (3 patients) were transient complications after the injections.

## Discussion

Duane syndrome is one of the congenital disorders with impaired cranial nerve innervations to the ocular rectus muscles. The deviation in this syndrome is usually treated by muscle recession in affected side or both eyes based on amount of deviation.<sup>6,9</sup> A low rate of amblyopia has been reported in Duane syndrome.<sup>10</sup> In contrast, our patients showed a 68.75% rate of amblyopia. This high rate may be explained by the referral nature of our hospital. Therefore, more severe cases were referred to our center.

In this study, dominance of the female gender and left eye involvement were in accordance with prior studies.<sup>11,12</sup> In some studies, a higher incidence of amblyopia was reported in bilateral Duane syndrome, probably as a result of more prevalence of anisometropia, vertical strabismus, and ametropia in bilateral cases, in contrast to the study of Zanin et al with a similar frequency in unilateral and bilateral cases.<sup>13,14</sup> While in our series 2 patients with bilateral involvement had amblyopia, we could not make any judgment about it because of the limited number of patients.

The treatment in this syndrome concentrates on the improvement of primary deviation and abnormal head posture, not on creating normal adduction or abduction.<sup>15</sup> A technique other than muscle surgery, like botulinum toxin injection, could be utilized to obtain the treatment's object.<sup>16,17</sup> In this procedure, there is a low possibility of surgical complications such as scleral perforation, postoperative conjunctival injection, granuloma and allergic reactions, scar and inclusion cyst of conjunctiva, adherence syndrome, change in palpebral fissure, dellen ulcer, and anterior segment ischemia.<sup>18</sup> The rate of complication after botulinum toxin injection is less common than surgery. Transient complications in our series such as ptosis, subconjunctival hemorrhage, and vertical deviation were also reported in prior studies.<sup>4,16</sup> In spite of these

transient complications, the permanent effect of botulinum could be obtained by repeated injections (2–3 times)<sup>16</sup> without creating any permanent degenerative or atrophy of muscle.<sup>19</sup>

Consequently, botulinum injection could be accepted as a quite safe treatment.

Despite the use of botulinum toxin injection in a wide spectrum of strabismus disorders, including congenital esotropia, acute paralytic strabismus, thyroid associated orbitopathy, and congenital nystagmus,<sup>20–25</sup> there is limited investigation in the clinical outcome of botulinum toxin injection in the patients with Duane syndrome.<sup>4,7</sup> The study of Dawson et al<sup>4</sup> is the chief investigation of efficacy of botulinum toxin injection in the treatment of Duane syndrome with 88 cases. They reported 53% reduction of deviation in the long-term. Our results, with 75% improvement (complete or partial) after botulinum toxin injection, were comparable to the results of the Merino et al<sup>26</sup> study with a 70.58% success rate after muscle recession in 17 patients. Thus, despite the temporary effect of botulinum toxin injection, it could be accepted as an alternative to surgery with fewer complications and a permanent effect with repeated injection.

One of the interesting results in this investigation was the significant relation between the success rate and amount of FDT. Better responses were observed in the presence of 1 or 2 + FDT. Therefore, successful results of botulinum toxin injection in Duane syndrome could be seen in mild to moderate fibrotic muscles. As a result, FDT could be a predictive factor for response to botulinum toxin.

The limitations of our study included a small number of the patients, lack of control group with muscle recession surgery, absence of special technique for injection in fibrotic muscles, and lack of long-term follow-up. Other drawbacks of this investigation were the lack of assessment of up- or downshoot and globe retraction. Due to the low age of most patients in our series, evaluation of the outcome of botulinum toxin injection on stereopsis was not possible.

In conclusion, neither complete improvement, nor lack of surgical requirement could be gained in patients with Duane syndrome with botulinum toxin injection. However, botulinum toxin could be accepted in Duane syndrome instead or associated with muscle recession with appropriate case selection. It may be concluded that patients with lower degrees of FDT had better response to botulinum toxin injection.

## References

1. Duane A. Congenital deficiency of abduction associated with impairment of adduction, retraction movement, contraction of the palpebral fissure and oblique movements of the eye. *Arch Ophthalmol*. 1905;34:133–145.
2. Farvardin M, Rad AH, Ashrafzadeh A. Results of bilateral medial rectus muscle recession in unilateral esotropic Duane syndrome. *JAAPOS*. 2009;13:339–342.
3. BCSC, vol 6, 2010–2011, page: 127–130.
4. Barbe ME, Scott WE, Kutschke PJ. A simplified approach to the treatment of Duane's syndrome. *Indian J Ophthalmol*. 2013 Dec;61(12):701–704.

5. Dawson EL, Maino A, Lee JP. Diagnostic use of botulinum toxin in patients with Duane syndrome. *Strabismus*. 2010 Mar;18(1):21–23.
6. Barbe ME, Scott WE, Kutschke PJ. A simplified approach to the treatment of Duane's syndrome. *Br J Ophthalmol*. 2004;88(1):131–138.
7. Talebnejad MR, Sahraian N, Eghtedari M. Management of Duane's syndrome with botulinum toxin injection. *Iranian J Ophthalmol*. 2008;20(3):10–14.
8. Sanjari MS, Falavarjani KG, Kashkouli MB, et al. Botulinum toxin injection with and without electromyographic assistance for treatment of abducens nerve palsy: a pilot study. *J Am Assoc Pediatr Ophthalmol Strabismus*. 2008;12:259–262.
9. Chua B, Johnson K, Donaldson C, et al. Management of Duane retraction syndrome. *J Pediatr Ophthalmol Strabismus*. 2005;42(1):13–17.
10. Kekunnaya R, Gupta A, Sachdeva V, et al. Duane retraction syndrome: series of 441 cases. *J Pediatr Ophthalmol Strabismus*. 2012;49:164–169.
11. Mohan K, Sharma A, Pandav SS. Differences in epidemiological and clinical characteristics between various types of Duane retraction syndrome in 331 patients. *J AAPOS*. 2008;12:576–580.
12. DeRespinis PA, Caputo AR, Wagner RS, et al. Duane's retraction syndrome. *Surv Ophthalmol*. 1993;38:257–288.
13. Zanin E, Gambarelli N, Denis DL. Distinctive clinical features of bilateral Duane retraction syndrome. *J AAPOS*. 2010;14:293–297.
14. Isenberg S, Urist MJ. Clinical observations in 101 consecutive patients with Duane's retraction syndrome. *Am J Ophthalmol*. 1977;84:419–425.
15. Fricke J, Neugebauer A, Russmann W. Surgical options in retraction syndrome. *Klin Monatsbl Augenheilkd*. 2006;223(1):42–47.
16. Glosner L, Benezra D. Injection of botulinum toxin into the oculomotor muscles in disorders of ocular motility. *Klin Oczna*. 1991;93(9):264–265.
17. Broniarczyk- Loba A, Omulecki W, Nowakowska O, et al. Using botulinum toxin diagnostic test in a case of bilateral strabismus – turk- Duane (STD) syndrome found during preparation for cataract surgery. *Klin Oczna*. 2004;106(4–5):666–669.
18. Rowe F, Noonan C. Complications of botulinum toxin and their adverse effects. *Strabismus*. 2009;17(4):139–142.
19. Borodic GE, Ferrante R. Effects of repeated botulinum toxin injections on orbicularis oculi muscle. *J Clin Neuro Ophthalmol*. 1992;12:121.
20. Talebnejad MR, Eghtedari M. Botulinum toxin-A injection in acute sixth nerve palsy. *Iran J Ophthalmol*. 2006;19(3):34–37.
21. Talebnejad MR, Poorhabibi A. Management of essential infantile esotropia with botulinum toxin. *Iran J Ophthalmol*. 2005;18(2):77–82.
22. Crouch ER. Use of botulinum toxin in strabismus. *Curr Opin Ophthalmol*. 2006 Oct;17(5):435–440.
23. Lennerstrand G, Nordbo OA, Tian S, et al. Treatment of strabismus and nystagmus with botulinum toxin type A. An evaluation of effects and complications. *Acta Ophthalmol Scan*. 1998;76(1), 27–7.
24. Bagheri A, Eshaghi M. Botulinum toxin injection of the inferior oblique muscle for the treatment of superior oblique palsy. *J AAPOS*. 2006;10(5):385–388.
25. Akbari MR, Ameri A, Keshtkar Jaafari AR, Arash Mirmohammadsadeghi A. Botulinum toxin injection for restrictive myopathy of thyroid-associated orbitopathy: success rate and predictive factors. *J AAPOS*. 2016;20:126–130.
26. Merino P, Merino M, Gómez De Liaño P, et al. Horizontal rectus surgery in Duane syndrome. *Eur J Ophthalmol*. 2012 Mar–Apr;22(2):125–130.