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Sustained improvement of reading symptoms following botulinum toxin A injection for convergence insufficiency

Jon Peiter Saunte, MD¹ and Jonathan M. Holmes, BM, BCh²

¹Department of Ophthalmology, Glostrup University Hospital, Copenhagen, DK, USA

²Department of Ophthalmology, Mayo Clinic, Rochester, MN, USA

Abstract

Introduction—We evaluated the use of botulinum toxin A in adults with convergence insufficiency in whom prior treatment had failed.

Methods—We studied 8 patients (median age 36 years, range 17 to 77 years) with reading symptoms due to convergence insufficiency defined as an exodeviation greater at near, not exceeding 10 PD in the distance measured by prism and alternate cover test, and either convergence near point >6 cm or reduced fusional amplitudes. All patients were still symptomatic after prior treatment by convergence exercises ($n = 8$), base-in prism glasses ($n = 5$) or strabismus surgery ($n = 2$). Five patients received injection of 5 IU botulinum toxin in 0.1 ml saline to one lateral rectus muscle, two received 2.5 IU, and one received 2.5 IU to both lateral rectus muscles.

Results—At 1 month post injection, all patients had an initial reduction of exodeviation from baseline (median 9 PD, $p = 0.008$) at near, although 2 patients had a temporary intermittent esotropia in the distance with diplopia associated with difficulty driving. At 6 months, when the pharmacological effect of botulinum toxin had completely worn off, patients still maintained a small reduction of exodeviation (median 4 PD, $p = 0.3$) at near. Reading symptoms improved in 7 of 8 patients at 1-month post injection, and in all patients at 6 months. Two patients had health-related quality of life assessed with the Adult Strabismus 20 Questionnaire, showing improved Reading Function scores at 6 months. Interestingly, 3 patients reported improved reading despite returning to the baseline angle at 6 months, and 2 of 4 with 12-month follow-up still reported improvement.

Conclusions—In adult convergence insufficiency, botulinum toxin injection to a lateral rectus muscle improves reading symptoms beyond the duration of the pure pharmacological effect. Botulinum toxin injection may be useful in management of adult convergence insufficiency, although repeat injections may be needed.

Keywords

Botox; Botulinum toxin; convergence insufficiency; reading function; strabismus

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Correspondence: Dr. Jonathan M. Holmes, Ophthalmology E4, Mayo Clinic, Rochester, MN 55905. Tel: (507) 284-3760. Fax: (507) 284-8566. holmes.jonathan@mayo.edu.

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INTRODUCTION

Convergence insufficiency is a common binocular vision disorder characterized by exophoria greater at near than at distance, and one or both of the following: a remote near point of convergence or decreased positive fusional vergence.¹ It is often associated with symptoms such as double vision, eyestrain, headaches, blurred vision, and loss of place while reading or performing near work.² Convergence insufficiency in adults has a peak incidence in the eighth decade of life,³ and commonly exists without any association of ocular or neurological disorders, but can be associated with head trauma, neurodegenerative diseases, cerebral ischemia, thyroid ophthalmopathy, myasthenia gravis, toxic agents or medications, infection, inflammation or decompression sickness.⁴ Management options for convergence insufficiency include base-in prisms,^{5,6} convergence exercises,⁷ psychotherapy, or even surgery.^{8,9,10} If surgery is performed, procedures include either recessions of the lateral rectus muscles, or resections of the medial recti muscles with or without slanting, but the surgical success rates varied from 18–92%.^{8,9,10} Because many types of treatment for convergence insufficiency are not always successful, alternative treatments are desirable.

The use of botulinum toxin type A for treating strabismus was first reported in 1980 by Scott,¹¹ but has only recently been described as a treatment option for intermittent exotropia of convergence insufficiency type by Dawson et al., and only in abstract form.¹² The purpose of the present study is to report outcomes in patients with convergence insufficiency treated by injecting botulinum toxin type A (BOTOX®, Allergan, Inc., Irvine, California) to a lateral rectus muscle. To our knowledge, treatment for convergence insufficiency with botulinum toxin has not been reported in the peer-reviewed literature (literature search: PUBMED 1966 to December 11, 2013, search term: botulinum toxin AND convergence insufficiency NOT esotropia NOT hypertropia NOT hypotropia NOT migraine).

MATERIALS AND METHODS

We retrospectively identified 8 patients (median age 36 years, range 17 to 77 years) with convergence insufficiency defined as an exodeviation greater at near, not exceeding 10 prism diopters (PD) in the distance measured by prism and alternate cover test (PACT), who all had symptoms of reading difficulty (Table 1). Six of eight patients had convergence near point beyond 6 cm (median 19 cm, range 10–100 cm). Of the remaining two patients, patient two (Table 1) did not meet Sheard's criterion⁵ (break point at near of 25 PD with an angle of 16 PD exophoria) consistent with the diagnosis of convergence insufficiency. Patient three had an exophoria greatest at near with apparently adequate fusional amplitudes, but had severe difficulties performing near tasks and reading, and was thus included in the study. Four patients were studied from each of the two authors' institutions. Two patients had a history of head trauma with subsequent onset of reading problems. All patients demonstrated measurable stereoacuity (range 40–240 arc sec) measured either by TNO (Lamérís Ootech BV, Ede, Netherlands) or the Randot Preschool Stereotest (Stereoptical Co. Inc., Chicago, IL). The patients in this study had received treatment for convergence insufficiency by base

in prisms ($n = 5$), convergence exercises for up to 4 years ($n = 8$) and/or strabismus surgery ($n = 2$), but were still symptomatic at the time of Botox injection.

Five patients received injection of 5 IU botulinum toxin in 0.1 ml normal saline to one lateral rectus muscle, 2 patients 2.5 IU to one lateral rectus muscle, and one received 2.5 IU botulinum toxin to both lateral rectus muscles. The injection was performed under local anesthesia in seven patients, and under general anesthesia in one patient. Four patients had injection assisted by electromyography, three patients had injection by grasping the lateral rectus muscle belly through the conjunctiva and then injecting the muscle, and one patient received injection via a conjunctival incision under general anesthesia (Table 1).

Evaluation of alignment and symptoms were recorded before botulinum toxin injection (baseline), after approximately 1 month (26–63 days), after approximately 6 months (84–207 days), and after approximately 12 months (360–545 days). We recorded the ocular alignment at near (30 cm) and distance (3 or 6 m) by PACT. The patients were instructed to report reading symptoms as worse, unchanged, improved, or recurred compared with baseline. Two patients also completed the health-related quality of life Adult Strabismus 20 (AS-20) Questionnaire.^{13,14} Statistical analyses on changes from baseline were performed using signed rank tests. (SAS, Version 9.3, SAS Institute Inc. Cary, NC). Both Mayo Clinic Institutional Review Board and The Danish Datatilsynet approval was obtained for this study. All procedures and data collection were conducted in a manner compliant with the Health Insurance Portability and Accountability Act and conformed to local laws and principles of the Declaration of Helsinki.

RESULTS

At baseline, the median near deviation was 17 PD exophoria (range 10 PD exophoria to 25 PD exophoria) and the median distance deviation was 4 PD exophoria (range 0 PD to 10 PD exophoria). All patients reported symptoms of difficulty reading at near. The Reading Function domain score of the AS-20 was available in two patients (scores of 13 and 20, where 0 is the worst and 100 is the best HRQOL).

At 1-month post injection, the median angle of deviation at near was 8 PD exophoria (range: 15 PD esophoria to 18 PD exophoria (Table 1)), which represented a median reduction in exodeviation from baseline of 9 PD (range: 2 PD reduction to 31 PD reduction, $p = 0.008$). At distance, the median angle of deviation was 0 PD (range 30 PD esophoria to 15 PD exophoria), with a median reduction in exodeviation of 2.5 PD (range 5 PD increase to 32 PD reduction, $p = 0.1$). Seven patients reported improved reading symptoms, and one patient was unchanged (Table 1). The Reading domain score of the AS-20 data was available for one patient, and the score improved from 20 to 69.

At 6 months post injection, the median angle of deviation at near was 11 PD exophoria (range: 16 PD esophoria to 30 PD exophoria (Table 1)), which represented a median reduction in exodeviation from baseline of 4 PD (range: 10 PD increase to 30 PD reduction, $p = 0.3$). At distance, the median angle of deviation was 1 PD exophoria (range: 25 PD esophoria to 12 PD exophoria), with a median improvement in exodeviation of 0.5 PD

(range 4 PD increase to 29 PD reduction, $p = 0.7$). All patients reported improved reading symptoms (Table 1). AS-20 data were available for two patients, and the scores improved from 20 to 85 in one patient, and from 13 to 20 in the second patient. At 6 months, all eight patients reported improved reading function, and interestingly, in three patients (patients 1, 5 and 7), the near angle of exodeviation had returned to baseline, but the reading symptoms were still improved.

Data at 12 months were available for four patients, the remaining patients had either not reached their 12-month follow-up time point or had moved away. For the 4 patients with follow-up, at 12 months post injection, the median angle of deviation at near was 9 PD exophoria (range: 16 PD esophoria to 35 PD exophoria (Table 1)), which represented a median reduction in exodeviation from baseline of 3 PD (range 10 PD increase to 30 PD reduction, $p = 0.6$). At distance, the median angle of deviation was 0 PD (range: 16 PD esophoria to 8 PD exophoria), with a median reduction in exodeviation from baseline of 1.5 PD (range 0 PD to 20 PD, $p = 0.3$). Two of four patients reported improved reading symptoms. The remaining two of four patients reported recurrent diplopia at near and expressed a desire for repeat injections.

Regarding side effects of botulinum toxin injections, two patients developed a moderate esodeviation greater at distance fixation (Table 1) with diplopia at distance, associated with difficulty driving and taking several months to resolve. One patient experienced 2 mm ptosis, which resolved 4 weeks post injection. No pupillary changes were reported. Visual acuity remained unchanged in all patients. No patients developed a new persistent vertical tropia.

DISCUSSION

In our series of patients with convergence insufficiency treated by botulinum toxin injection, we found an initial improvement in exodeviation, which was associated with a prolonged improvement in reading symptoms. The reading symptoms were improved in seven of eight patients at 1 month post injection, and in all patients at 6 months post injection, well beyond the 3-month duration of the chemical effect of botulinum toxin. Interestingly, improvement in reading symptoms was reported by all eight patients despite the deviation returning to baseline at 6 months post injection in three patients, and even at 12 months, there was reported improvement in reading symptoms by two of four patients.

Scott introduced using botulinum toxin to treat strabismus in 1980,¹¹ and recently Dawson et al presented a poster describing the treatment of convergence insufficiency type intermittent exotropia with botulinum toxin (Dysport).¹² In Dawson's study, 10 patients received botulinum toxin injections to a single lateral rectus muscle, and 80% had improvement 2 to 3 weeks later, but the abstract does not report specific data on reading symptoms.

Botulinum toxin blocks neuromuscular transmission, and when injected intramuscularly at therapeutic doses, the toxin produces partial chemical denervation of the muscle resulting in a localized reduction in muscle activity, which lasts up to 3 months.¹⁵

In our cohort we observed improved reading symptoms even though the alignment had returned almost to baseline in some patients at 6 months and beyond. A similar phenomenon has been reported in patients with convergence insufficiency who perform convergence exercises and enjoy a prolonged effect on reading symptoms despite no significant change in angle after tapering convergence exercises.¹⁶ After convergence exercises, improvement in reading has been attributed to improved fusional vergence. It is possible that improvement in vergence occurred in our patients as well, but this was not measured systematically in our study.

The usual explanation for a prolonged effect of botulinum toxin is a permanent change in deviation caused by changes in muscle sarcomere length.^{17,18} These changes may be mediated by a differential effect on orbital and global muscle fibers. Injection to the orbital part of the rectus muscle causes a reduction in the functional capacity of the primarily singly-innervated orbital muscle fibers, versus less effect on the primarily multiply-innervated global fibers.¹⁹ Our finding of a prolonged effect on reading may also be mediated by such changes in the antagonist muscle without a change in angle. The force generated by the antagonist muscle may be greater months after the effect of botulinum toxin on the agonist has worn off. The improved reading may also be explained by reduction of the number of mitochondria in the singly-innervated muscle fibers in the orbital portion of the rectus muscle.²⁰ The reported loss of mitochondria in rectus muscles injected by botulinum toxin²⁰ may translate into increased fatigue of the injected lateral rectus muscle, thus improving convergence. Despite uncertainty regarding mechanism, it is noteworthy that improvement of reading function was prolonged in our patients receiving botulinum toxin injection for convergence insufficiency.

There are some limitations to the present study. This study is a retrospective study of a heterogeneous patient population with a small sample size with a short follow-up time. We do not yet have sufficient length of follow-up to report how often repeat injections are needed, but 2 of our patients with 12 months of follow-up continued to express improvement in reading symptoms and 2 patients requested repeat injection at 12-months. The etiology of the convergence insufficiency cohort was not the same in all patients; two had onset after head trauma, the other six patients had convergence insufficiency of unknown etiology. Two of the patients had prior strabismus surgery for their convergence insufficiency, and all patients had previously performed convergence exercises without improvement of symptoms. The injected dose of botulinum toxin varied within our cohort, one patient received injections to both lateral recti muscles and the other 7 had injection to one lateral muscle. Data on convergence fusion amplitudes and convergence near point were also not available in all patients in this study. The measurements of reading symptoms were not standardized. Future studies should use standard measures of reading symptoms, e.g. the AS-20 questionnaire.^{13,14} Finally, we cannot rule out a placebo effect of injection because there was no control group.

Botulinum toxin injections may be useful in the management of convergence insufficiency in adults. The treatment is quick, safe, and can be performed in an outpatient clinic. The costs per injection can be reduced if several patients are treated on the same day. The effect on reading symptoms in convergence insufficiency patients may last more than 6 months,

and injections can be repeated for recurrent symptoms if needed. Some of our patients developed a moderate angle esodeviation with diplopia particularly in the distance, which interfered with driving for several months, and so patients should be warned of this potential problem prior to treating convergence insufficiency with botulinum toxin. Because not all patients with convergence insufficiency do respond to treatment with convergence exercises or base-in prisms, a single injection of botulinum toxin to a lateral rectus muscle might be a useful alternative. The reported long-lasting improvement in reading symptoms in the present study is encouraging, and additional prospective studies are needed to further evaluate this treatment option for patients with convergence insufficiency.

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TABLE 1

Subject Demographics, Clinical Features, and Outcomes

Pt no	Age	Botox Dose IU	Method	Pre Injection (Baseline)			1 Month post injection			6 Months post injection			12 Months post injection		
				Angle Near*	Angle Distance*	Reading Symptoms	Angle Near*	Angle Distance*	Reading Symptoms	Angle Near*	Angle Distance*	Reading Symptoms	Angle Near*	Angle Distance*	Reading Symptoms
1	29	5	Open	20 X	8X 2RH	Double	6 X	1 X	Improved	25 X 2RH	12X 4RH	Improved			
2	30	5	Closed	16 X	2 X	Double	15 E(T)	30 E(T)	Improved	0 X	0 X	Improved			
3	34	5	Closed	14 X	4 X	Double	14 E(T)	20 E(T)	Unchanged	16 E(T)	25 E(T)	Improved	16 E(T)	16 E(T)	Recurred
4	67	5	Closed	18 X	4 X	Double	10 X	1 X	Improved	12 X	2 X	Improved			
5	38	5	EMG	20 X	8 X	Double	18 X	6 X	Improved	30 X	8 X	Improved			
6	17	2.5	EMG	10 X	0 X	Double	0 X	0 X	Improved	6 X	0 X	Improved	6 X	0 X	Improved
7	77	2.5 Bilat.	EMG	25 X	10 X	Double	18 X	15 X	Improved	25 X	12 X	Improved	35 X	8 X	Recurred
8	73	2.5	EMG	14 X	1 X	Double	10X2LH	0 X 2LH	Improved	10 X	0 X	Improved	12 X	0 X	Improved

IU = International Units, X = exophoria, E(T) = intermittent esotropia, R = right, L = left, H = hyperphoria.

* Measured with prism and alternate cover test (PACT)