Botulinum toxin A in the treatment of paralytic strabismus

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Abstract
The purpose of the study was to assess the results of botulinum neurotoxin type A (BoNT/A) treatment in paralytic strabismus, particularly its value in determination of optimal surgical approach and a possible adjunct to conventional surgery. The design of the study was an interventional case series. Three patients with acquired VI nerve palsy were treated. The third one had a restrictive hypodeviation, as well. Injection of BoNT/A (Dysport®), 5 m.u. with an “open sky” technique and without the aid of electro–myographic control into the medial rectus muscle (MRM) was initially performed in first 2 patients, while the last one underwent a bilateral MRM (5 m.u.) and combined right inferior rectus muscle botulinum toxin injection (7.5 m.u.) with large recession after accessible adhesion dissection. General endotracheal balanced anesthesia was used. All patients gained some benefit from injection of BoNT/A, either therapeutic or diagnostic, or both. Unique characteristics of BoNT/A make it not so much an alternative to surgery as a complementary treatment or a possible valuable diagnostic tool in surgical planning in paralytic strabismus.

Key words: Botulinum Toxin Type A, Paralytic Strabismus

Introduction
Botulinum toxin is produced by Clostridium botulinum, which is a gram–positive anaerobic bacterium. The organism can produce 8 strains of antigenically different neurotoxins.

The German physician and poet Justinus Kerner (1786–1862) first developed the idea of a possible therapeutic use of botulinum toxin, which he called “sausage poison”. In 1973, Alan Scott, used botulinum neurotoxin type A (BoNT/A) in monkey experiments, and, in 1979, he introduced the therapeutic use of BoNT/A to treat strabismus1. Subsequent studies showed that BoNT/A is safe and offers a number of indications for certain types of strabismus, especially acquired VI nerve palsy. It can be a useful therapeutic tool and in certain cases it has diagnostic value2. BoNT/A causes a temporary paralysis of the injected muscle, resulting in reduced or even reversed deviation due to unopposed action of the ipsilateral antagonist muscle. It was considered as the most radical innovation in the management of strabismus since the introduction of surgery in 18393. In spite of a quarter of the century long therapeutic experience, and known advantages and disadvantages, clear guidelines for the treatment of various types of strabismus are still missing at this time.

Our aim is to assess the results of BoNT/A treatment in paralytic strabismus, particularly its value in determination of optimal surgical approach and a possible adjunct to conventional surgery.

Our patients
Three patients were treated.

Case 1
History
A 30 year old women sustained blunt head trauma in a motor vehicle accident 17 months earlier.

Examination
Visual acuity is 6/6 in each eye. In the primary position there is a large left esotropia, approximately 60 prism diopters (PD), with 10 PD left hypertropia. The left eye (LE) can not abduct to the midline. In addition depression of the LE is slightly limited. Versions are normal in the left gaze. Passiveduction testing shows severe restriction, allowing abduction slightly over the midline. With extreme left face turn and right gaze single binocular vision is achieved.

Diagnosis
Traumatic chronic left sixth nerve paralysis (Fig. 1).

Case 2
History
A 22 year old women had a brain tumor surgery (Astrocytoma pilocyticum fossae crani posterioris) 7 years ago. Her right eye (RE) crossed moderately after the surgery.

Examination
With the LE fixing, approximately 50 PD of right esotropia is noted. When fixing with the RE the deviation increases.
The RE moves beyond the midline, with slightly reduced saccadic velocity during abduction. Forced duction testing shows some restriction to full abduction of the RE.

**Diagnosis**

Chronic incomplete right sixth nerve paralysis (Fig.2).

**Case 3**

**History**

A 31 year old women had a multiple brain tumor surgery (Chordoma basseos cranii), as well as several facial bones reconstructive procedures for the past several years. After the fourth procedure she noticed that the RE crossed moderately, with significant loss of visual acuity. In addition, following orbital floor chondroplasty her RE crossed completely and downwards. 2.5 months after the additional tumor tissue extirpation and subsequent irradiation therapy she noticed limitation of abduction of the LE. Four months after that event she is concerned about her better LE, as well as a possibility of improving alignment of the RE.

**Examination**

Corrected visual acuity is 2/60 OD and 6/5 OS. In the primary position, the RE is extremely esodeviated and largely hypodeviated. Elevation and abduction of the RE are severely limited. Abduction of the LE is moderately limited. Passive duction testing reveals severely limited elevation and abduction in the RE and slight limitation to abduction in the LE. Right descedent optic nerve atrophy is present.

**Diagnosis**

Chronic right sixth nerve palsy with restrictive hypodeviation. Subacute incomplete left sixth nerve paralysis (Fig.3).

**Intervention**

Injection of BoNT/A (Dysport®), 5m.u. under direct visualization with an “open sky” technique and without the aid of electro-myographic control into the medial rectus muscle (MRM) was performed in first 2 patients, while the last one underwent a bilateral MRM (5m.u.) and combined right inferior rectus muscle botulinum toxin injection (7.5m.u.) with large recession after accessible adhesion dissection. General endotracheal balanced anesthesia was used.

**Results**

**Case 1**

Fifteen days after BoNT/A injection, there was no apparent improvement except for some relief of MRM contracture by forced duction testing (Fig.4).

An additional full tendon transposition of the vertical recti with traction sutures for 7 days was done. Small left exotropia with some abduction. One month after transposition surgery, abduction is decreasing (Fig.5). 4.5 months after surgery, there is left 35 PD esotropia with small (4 PD) hypertropia in primary position (Fig.6). Inability to abduct the LE beyond the midline.

**Case 2**

Fifteen days after BoNT/A injection, there was slight improvement of deviation and abduction, with almost complete relief of MRM contracture (Fig.7).

**Case 3**

Fifteen days after BoNT/A injections and right inferior rectus surgery, there was a small eso and hypodeviation of the RE, full abduction of the LE, decreased adduction of the RE (Fig.8). One and a half month after the intervention, a slight decrease of RE abduction and increase of esodeviation were noted (Fig.9). Five months after the intervention, there was further decrease of abduction and increase of eso and hypodeviation of the RE. Abduction of the LE remained unchanged (Fig.10).

**Further treatment**

For the first subject our plan is additional adjustable MRM recession 6 months after transposition surgery, once the anterior segment circulation stabilizes. For the second, adjustable recession–resection procedure after wearing on the BoNT/A effect, 6 months after the injection. The last one will require adjustable right MRM recession combined with adjustable lateral rectus tuck with the trial of additional dissection of scar tissue and inferior rectus recession, and an extensive conjunctival recession.

**Discussion**

In a patient with a chronic, particularly a sixth nerve palsy, BoNT/A injection of the MRM may allow enough relaxation of contracture to permit the partially paretic muscle to recover a normal range of action. This can lead to a cure with normal ocular motility. This was the rationale for injection particularly for the second subject. For the first subject, BoNT/A injection allowed transposition surgery that will be followed with additional MRM surgery, once the anterior segment circulation stabilizes. The third subject obviously took the most advantage of BoNT/A injection. Subacute sixth nerve palsy of the LE was cured completely. It wasn’t a significant possibility that it would cure spontaneously after 4 months. She avoided surgery on her left only functional eye, and also in conjunction with additional surgery is going to improve the appearance of the RE.

**Conclusions**

Unique characteristics of BoNT/A make it not so much an alternative to surgery as a complementary treatment or a possible valuable tool in surgical planning in paralytic strabismus.
Botulinum Toxin Type A, Paralytic Strabismus

**Figure 1.** Case 1. Left sixth nerve paralysis.

**Figure 2.** Case 2. Incomplete right sixth nerve paralysis.

**Figure 3.** Case 3. Right sixth nerve palsy with restrictive hypodeviation. Incomplete left sixth nerve paralysis.

**Figure 4.** Case 1, fifteen days after BoNT/A injection.

**Figure 5.** Case 1, one month after transposition surgery.

**Figure 6.** Case 1, 4.5 months after surgery.
References

Botulin toksin A u lečenju paralitičkog strabizma

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Kratak sadržaj

Cilj rada je bila procena vrednosti primene botulin neurotoksina A (BoNT/A) u lečenju paralitičkog strabizma, posebno njegovog značaja u određivanju optimalnog pristupa i moguće dopune konvencionalnoj hirurškoj intervenciji. Studija je dizajnirana kao interventna serija slučajeva. Lečene su tri bolesnice sa stečenom paralizom VI kranijalnog nerva. Treća bolesnica je, osim toga, imala i restriktivnu hipodevijaciju. Prve dve bolesnice su inicijalno dobile injekciju 5m.u., BoNT/A (Dysport®), u unutrašnji pravi mišić “open sky” tehnikom, bez elektro–miografske kontrole, dok je kod poslednje dato 5m.u. u oba unutrašnja prava mišića i urađena je velika retropozicija desnog donjeg pravog mišića posle disekcije dostupnih adhezija, kombinovana sa injekcijom 7.5m.u. BoNT/A. Primijenjena je opšta balansirana endotrakealna anestezija. Svi pacijenti su imali koristi od primene BoNT/A, bilo u terapijskom ili dijagnostičkom smislu, ili u oba. Jedinstvene karakteristike BoNT/A ga ne čine toliko alternativom hirurškom lečenju, već pre svega komplementarnim tretmanom ili mogućim vrednim dijagnostičkim postupkom u planiranju hirurškog pristupa kod paralitičkog strabizma.

Ključne reči: Botulin neurotoksin A – paralitički strabizam.