

(02)

Botulinum toxin injection as primary treatment for esotropia in patients with cerebral palsy

Iniekcje toksyny botulinowej jako zasadnicze leczenie zezu zbieżnego u pacjentów z mózgowym porażeniem dziecięcym

Mrugacz Małgorzata¹, Kulak Wojciech², Bakunowicz-Łazarczyk Alina¹, Bossowski Artur³

¹ Department of Pediatric Ophthalmology, Medical University of Białystok, Poland
Head: Professor Bakunowicz-Łazarczyk Alina, M.D., Ph.D.

² Department of Pediatric Neurology and Rehabilitation, Medical University of Białystok, Poland
Head: Professor Kulak Wojciech, M.D., Ph.D.

³ Department of Pediatric Endocrinology, Diabetology with Cardiology Division, Medical University of Białystok, Poland
Head: Professor Bossowski Artur, M.D., Ph.D.

Streszczenie:	<p>Cel: toksyna botulinowa typu A jest potencjalną neurotoksyną, która blokuje uwalnianie acetylocholiny z zakończeń cholinergiczných. Celem pracy jest ocena skuteczności iniekcji toksyny botulinowej w leczeniu zezu zbieżnego u pacjentów z mózgowym porażeniem dziecięcym.</p> <p>Materiał i metody: u 7 pacjentów z mózgowym porażeniem dziecięcym wykonano badanie okulistyczne i ortoptyczne. Iniekcję z toksyny botulinowej wykonano do mięśnia prostego przyśrodkowego w znieczuleniu ogólnym.</p> <p>Wyniki: średni wiek pacjentów wynosił 12 lat. U 57,1% pacjentów uzyskano poprawę w postaci równoległego ustawienia gałek ocznych (ortoforia \pm 10 PD).</p> <p>Wnioski: zastosowanie toksyny botulinowej w leczeniu zezu zbieżnego u dzieci i młodzieży z mózgowym porażeniem dziecięcym stanowi alternatywną metodę leczenia do konwencjonalnego postępowania chirurgicznego.</p>
Słowa kluczowe:	dzieci, choroba zezowa, zez zbieżny, toksyna botulinowa typu A.
Summary:	<p>Purpose: Botulinum toxin type A is a potent neurotoxin that blocks the release of acetylcholine at the neuromuscular junction of cholinergic nerves. Cerebral palsy is cause of ocular disorders. There is an increased presence of strabismus, refractive errors, and reduced visual acuity. The purpose of this study was to assess the efficacy of botulinum toxin injection in the treatment of esotropia in patients with cerebral palsy.</p> <p>Material and methods: Seven patients were included in the study. All patients had a full ophthalmic examination on initial visit, including cycloplegic refraction and duction. The angle of esotropic deviation at distance was recorded in prism diopters. The botulinum toxin type A was administered into the medial rectus muscle under general anesthesia.</p> <p>Results: Mean age of the patients was 12 years. The mean angle of deviation pretreatment was 36.6 PD. Successful motor alignment (orthotropia \pm 10 PD) was achieved in the botulinum toxin type A group in 57.1% of patients.</p> <p>Conclusions: The use of botulinum toxin in the treatment of esotropia in children and adolescents with cerebral palsy is an alternative to conventional surgical therapy.</p>
Key words:	children, strabismus, esotropia, botulinum toxin type A.

Cerebral palsy (CP) is the most common physical impairment in pediatrics with a frequency of approximately 2 to 2.5 per 1,000 live births in Western populations. The common core essential feature of CP is early-onset of motoneuron impairment that is the result of a non progressive pathology in the not-yet mature brain (1, 2).

Cerebral palsy is cause of ocular disorders. Visual impairments and disorders of ocular motility are common in children with CP. The use of botulinum toxin type A (BTXA) for strabismus was first described and developed by the American ophthalmologist Dr Alan Scott in the early 1980s (3). The toxin is produced by *Clostridium botulinus*, and causes paralysis by preventing the release of acetylcholine from motor nerve terminals, so it must be injected into the muscle close to these. The effect is a functional denervation of muscle; and the degree of paralysis is dose-dependant, and reversible as the nerves generate new neuromuscular junctions by terminal

sprouting and the formation of new end plates (4). BTXA is injected directly into the selected extraocular muscle. The effect of BTXA will start to be seen within 2–4 days of the injection, it then causes an overcorrection for some weeks (the effect), which then wears off after 6–8 weeks leaving a permanent realignment (the after-effect) in many cases.

The aim of this study was to assess the efficacy of the botulinum toxin in the treatment of esotropia in children and adolescents with cerebral palsy.

Methods

The study was approved by The Ethics Committee of Medical University of Białystok. Participants included all new patients with a nonparalytic, nonaccommodative constant esotropia who were seen in the Department of Pediatric Rehabilitation Medical University

of Białystok. Eligibility criteria included presence of esophoria and normal ductions. Exclusion criteria included presence of vertical deviations, A or V pattern before treatment, dissociated deviation before treatment, variable angle esotropia, and the presence of other ocular abnormalities.

All patients had a full ophthalmic examination on initial visit, including cycloplegic refraction and duction. The angle of esotropic deviation at distance was recorded in prism diopters (PD). Once the diagnosis was made, parents or legal guardians were offered treatment with BTXA injection or surgery, and informed consent was signed. Injections of BTXA (Dysport, Ipsen Limited, UK), were administered without conjunctival incision under general anesthesia with the use of inhalation of sevoflurane. The dose of BTXA ranged from 10 to 20 IU in 0.1 mL of saline depends on the angle of the esotropic deviation. Injections were performed without EMG guidance. Reinjection was offered whenever the patients had not orthotropia between 1 and 6 months after the last injection, for up to 2 additional doses.

Results

The age of patients ranged from 7 to 15 years, with an average 12.4 ± 6.5 years. The clinical characteristics of these patients are presented in Table I.

No of patients/ liczba pacjentów n = 7	Mean (SD)/
Age at treatment (years)/ Wiek leczenia (lata)	12.4 (6.5)
Sex, male (%) / Płeć, męska (%)	61.5
Prematurity (%) / Wcześnieactwo (%)	17.1
Pretreatment angle of deviation (PD)/ Kąt zeza przed leczeniem (DP)	36.9 (9.7)
Orthotropia (%) / Ortoforia (%)	56.5

Tab. I. Characteristics of cerebral palsy patients that received botulinum toxin injection as primary treatment of strabismus.

Tab. I. Charakterystyka pacjentów z mózgowym porażeniem dziecięcym, u których zastosowano iniekcje z toksyny botulinowej do leczenia choroby zezowej.

The mean angle of deviation pretreatment was 36.6 PD. Successful motor alignment (orthotropia ± 10 PD) was achieved in 57.1% of patients. All patients had a follow up at from 18 to 24 months. 3 patients (42.8%) received 1 injection, 1 patient (14.4%) 2 injections, and 3 patients (42.8%) received 3 injections to achieved a successful motor outcome.

Discussion

BTXA may be particularly useful in situation where strabismus surgery is undesirable, especially in young patients with unstable clinical status such as the patients with cerebral palsy. To treat esotropia, BTXA injection can be used into medial rectus and in exotropia injection can be done into the lateral rectus muscle. However, the use of BTXA in exotropia has been less successful than in esotropia. For small to moderate angle esotropia, BTXA was found to be as effective as one strabismus treatment in achieving alignment in a study of over 230 patients and was shown to be a reliable treatment option in various other studies (5). However, for large angle esotropia, BTXA is considered to be less effective and surgery should be considered instead (5, 6).

A prospective cohort followed by the Congenital Esotropia Observation Study showed that 89% of patients treated surgically were within 10 PD of orthophoria by the time they were 4.5 years of age but that 25% of patients had required at least one additional surgical procedure to achieve adequate horizontal alignment (7).

The reported rate of successful treatment esotropia with BT-A varies widely. In contrast to surgery, there are no data on the stability of alignment during the course of 5 or 10 years. Scott et al. observed a success rate of 66% in a subset of patients with infantile esotropia (8). Mc Neer et al. (9) reported a high success rate of alignment over 80% in patients with infantile esotropia but small to moderate angle of deviation followed for 3 years.

Our results are closer to the study by Campomanes et al. (5) on infantile esotropia, who obtained 59% of final success using BT-A and in 60% of standard surgery patients. All of our patients needed general anaesthesia because their clinical condition was evolving or unstable.

In summary, this study indicates that the use of botulinum toxin in the treatment of strabismus in children with cerebral palsy is an alternative to conventional surgical therapy. Botulinum toxin injection plays an important role in achieving balanced muscle function.

References:

- Rosenbaum P, Paneth N., Leviton A., Rosenbaum P, Paneth N., Leviton A.: *A report: The definition and classification of cerebral palsy April 2006*. Dev. Med. Child Neurol. 2007; 49: 8–14.
- Shevell M., Miller S., Scherer S.W., Yager J.Y., Fehlings M.G.: *The Cerebral Palsy Demonstration Project: A Multidimensional Research Approach to Cerebral Palsy*. Semin. Pediatr. Neurol. 2011; 18: 31–39.
- Scott A.B.: *Botulinum toxin injection of eye muscles to correct strabismus*. Trans. Am. Ophthalmol. Soc. 1981; 79: 734–770.
- Gordon N.: *The role of botulinum toxin type A in treatment - with special reference to children*. Brain & Development 1999; 21: 147–151.
- Dawson E.L., Lee J.P.: *Does Botulinum toxin have a role in the treatment of small-angle esotropia?* Strabismus 2004; 12: 257–260.
- Campomanes A.G.A., Binenbaum G., Eguiarte G.C.: *Comparison of botulinum toxin with surgery as primary treatment of infantile esotropia*. J. AAPOS 2010; 14: 111–116.
- Birch E., Stager D., Wright K., Beck R.: *The natural history of infantile esotropia during the first six months of life: Pediatric Eye Disease Investigator Group*. J. AAPOS 1998; 2: 325–328.
- Scott A.B., Magoon E.H., McNeer K.W., Stager D.R.: *Botulinum treatment of strabismus in children*. Trans. Am. Ophthalmol. Soc. 1989; 87: 174–180.
- McNeer K.W., Tucker M.G., Spencer R.F.: *Botulinum toxin management of essential infantile esotropia in children*. Arch. Ophthalmol. 1997; 115: 1411–1418.

The study was originally received 23.11.2012 (1421)/
Praca wpłynęła do Redakcji 23.11.2012 r. (1421)
Accepted for publication 13.12.2012/
Zakwalifikowano do druku 13.12.2012 r.

Reprint requests to (Adres do korespondencji):
dr hab. n. med. Malgorzata Mrugacz
Department of Pediatric Ophthalmology, Medical University
of Białystok, Poland
17 Washington Street
15-274 Białystok
e-mail: malgorzata.mrugacz@umb.edu.pl