

# **Treatment of Blepharospasm, Hemifacial Spasm and Strabismus with Botulinum A Toxin**

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Thirty patients with blepharospasm, hemifacial spasm, strabismus and entropion were treated with botulinum A toxin giving satisfactory results. Rapid spasm relief, correction of strabismus and entropion were obtained. Only mild, transient and local side effects occurred. The patients were followed up for 4 – 12 weeks with no recurrence. The clinical results show that local injection of a minute dose of botulinum A toxin in treating blepharospasm, hemifacial spasm, strabismus and entropion is a safe, effective and simple method of nonsurgical therapy.

Blepharospasm and hemifacial spasm commonly seen in ophthalmological and neurological clinics, are chronic, progressive neuromuscular disorders often occurring in the middle-aged and the aged. Frequent and prolonged spasmodic contracture of the eyelids and facial muscles and involuntary closure of the eyelids may result in visual disturbance or even functional blindness. This inconveniences patients and may distort the facial appearance. Different treatments using drugs, surgery, biofeedback, acupuncture and moxibustion have been prescribed with little avail. Since botulinum A toxin injection was introduced by Scott, USA for the treatment of strabismus<sup>[1]</sup>, this toxin has been developed for the treatment of blepharospasm, hemifacial spasm and entropion with good results.<sup>[2, 3]</sup>

On the basis of successful experiments on animal models (monkeys)<sup>[4]</sup>, a crystalline botulinum A toxin developed in the Lanzhou Institute of Biological Products and approved by the Chinese Ministry of Public Health for clinical study has been used in eyelid and hemifacial spasms, strabismus and entropion with satisfactory results.

## **Patients and Methods**

**Patients:** A group of 30 patients, 20 males and 10 females, aged 19 to 80 years, had histories of illness for one month to 38 years. Nineteen patients had hemifacial spasm associated with blepharospasm, unilateral blepharospasm, bilateral blepharospasm, 1 right paralytic exotropia, 1 disabled exotropia, 5 concomitant strabismus, and senile lower eyelid entropion and 1 cicatricial lower eyelid entropion.

These patients had undergone either medicinal, surgical or acupuncture treatment without effect.

**Methods:** *Before and after treatment.* The patients were examined for eyelid position and spasmodic intensity. Slit-lamp examination and cover-uncover test using corneal reflex and prism neutralization were done to determine strabometric degree. Some patients were photographed and videotaped before and after treatment. Follow-up examinations were given twice weekly in the first two weeks, once weekly in the next two weeks and once every month thereafter for a total 12 weeks.

*Dosage and administration.* The crystalline botulinum A toxin, developed for clinical use by the Lanzhou Institute of Biological Products, is a freeze-dried crystalline toxin, lot number 9002 was packed in ampoules of 180 units; each unit equivalent to 1 LD<sub>50</sub> (white mouse) containing 0.04 ng toxin, kept at -20 °C in a freezer or in the deep freeze compartment of a refrigerator. When diluted in sterile normal saline to the appropriate concentration, it was used for local injection into orbicularis oculi, face or eye muscles, bilaterally or unilaterally as required, at single or multiple sites, with a volume of 0.1ml at each site (containing a toxin dose of 2 to 2.5 units). Four or five sites were used inside and outside of the upper or lower eyelid or to the orbicularis oculi at the temporal side of the outer canthus. For hemifacial spasm, 3 more sites were chosen at middle and lower face muscles and at cheek muscles in addition to the above sites. The total dosage was an algebraic sum of all sites. One or two reinjection were applied at an interval of several days if there was residual spasm; the dosage was chosen as the spasmodic intensity required. A TB syringe with its needle was used for the injections. For strabismus, the toxin dosage was determined by the factors of strabismic deviation, age and weight with an additional initial dose of 0.2 U/kg of body weight. Generally, a volume of 0.1 ml was injected into each muscle. One reinjection may be given at an interval of several days if there is residual strabismus. A TB syringe with a special needle of 27 gauge or 5 gauge was used for injection into the eye muscle under the guidance of a specialized EMG amplifier.

**Efficacy criteria and assessment:** Blepharospasm and hemifacial spasm were graded and assessed in terms of their intensity on a scale of 0 – IV as follows: 0 = no spasm; I = increased blinking caused by external stimuli; II = slight fluttering of eyelids and facial muscles without functional disturbance; III = moderate, marked spasm with mild functional disturbance; IV = severe spasm and functional disturbance, affecting such daily activities as driving, reading, etc.

Strabismus and entropion were assessed in terms of the degree of their correction.

## Result

In 21 patients with blepharospasm and hemifacial spasm, clinical observations showed marked improvement in symptoms starting 24 hours after the injection and rapid relief within 2 – 11 days. Of the 21 patients, 19 were improved to Grade 0 (90.5%) and 2 were improved to Grade I (9.5%) from their pretreatment Grades II – IV. Of the 7 patients with strabismus, 5 were completely corrected to normal position and two were basically corrected (Table). Two patients with lower eyelid entropion were completely corrected. In both cases, the correction was effected within 4 – 6 days. After botulinum A toxin injection, the effect lasted for a minimal period of 10 weeks and a maximal of over 12 weeks (long-term effect still under observation).

In all the injected patients, no systemic side-effects were observed and no abnormal results were reported in liver function test and routine urine examinations before and after treatment in some patients. However, mild and transient side-effects may occur at parts of the eye. For example, of the patients with blepharospasm and hemifacial spasm, one had had ptosis which spontaneously normalized in 7 days and two had had lagophthalmus which normalized in 3 – 21 days. In the case of concomitant esotropia, ptosis was prone to occur but not in the case of exotropia. After treatment, all the patients felt remarkably improved and relieved of subjective symptoms and objective signs with functional recovery and significant improvement in appearance.

**Toxin injection effects in strabismus**

Serial No.	Strabismus	Prism diopter		Side effect (ptosis)
		Before injection	After injection	
1	Paralytic exotropia	30 – 40 <sup>Δ</sup>	Normal position	No
2	Disabled exotropia	30 <sup>Δ</sup>	Normal position	No
3	Concomitant exotropia	30 <sup>Δ</sup>	Normal position	No
4	Concomitant exotropia	30 <sup>Δ</sup>	Normal position	No
5	Concomitant exotropia	60 <sup>Δ</sup>	Normal position	Yes
6	Concomitant exotropia	60 <sup>Δ</sup>	20 <sup>Δ</sup>	Yes
7	Concomitant exotropia	90 <sup>Δ</sup>	20 – 30 <sup>Δ</sup>	Yes

## Discussion

Blepharospasm and hemifacial spasm are common neuromuscular spasmodic disorders involving ophthalmology, neurology, otorhinolaryngology and stomatology, and are not uncommonly seen among the middle-aged and the aged both at home and abroad. In China, as neither medical nor surgical treatments were effective, patients often gave up treatment. Strabismus is often seen in children with a morbidity of about 3%. In the past, surgery was the treatment of choice but often the patients were not able to have surgery in time to cure the disability. To protect the patients' eye sight, we have for the first time in China carried out this study of nonsurgical treatment of strabismus using drug injection into extraocular muscles.

In this study, the nonsurgical treatment of blepharospasm, hemifacial spasm and strabismus was done by local drug (botulinum A toxin) injection directly into the effectors eyelid (orbicularis oculi), facial muscles or muscoli oculi, to act directly on the endings of peripheral motor nerves to relive muscular spasm or lessen muscular function by effecting flaccid paralysis of the muscles instead of acting on facial nerve trunk or branch. The drug-crystalline botulinum A toxin used in this study is a neurotoxin of macro-molecular protein obtained from culture of clostridium botulinum. The mechanism of action is to inhibit release of acetylcholine at peripheral motor nerve terminals and at neuromuscular junctions, resulting in muscular relaxation and paralysis and relief of eyelid or facial muscular spasm or change in eye position and finally correction of strabismus. It can also be used to correct such muscular spasms as entropion, tortillis, etc. as observed by some investigators, botulinum A toxin may affect the nutrition of muscles by nerves causing muscular trophia, but it was also noted that there was regeneration and redistribution of terminal plates of peripheral mortor nerve endings, so reinjection should be given for recurrence of muscular spasm after some months of toxin injection. It appears to be a favorable factor for treatment of strabismus.

Our clinical observations show that all 30 patients treated in this series achieved satisfactory results, in conformity with the mechanism of muscular paralysis brought about by botulinum A toxin, with rapid relief of muscular spasm and correction of strabismus and lower eyelid entropion. Of 21 patients with blepharospasm and hemifacial spasm, 19 showed marked improvement (90.5%) and 2 improvement (9.5%).

The advantages of this therapy are rapid spasmodic relief shortly after injection, long-term drug-efficacy allowing 10 – 12 weeks or more before another injection, no

pain during treatment, and simple, easy method suitable for clinical application and acceptability to the public. For strabismus, the injection needs only topical anesthesia and guidance of EMG amplifier. It is a painless and safe procedure and is especially suitable for patients with anesthesia contraindication and dislike or refusal of surgery. This therapy produces no systemic reactions, only some mild and naturally relievable side-effects. Reinjection induces no allergic reaction. Mild ptosis or lagophthalmos was seen in a few cases after drug injection dosage, accuracy of injection and individual differences which need further study to reduce their occurrence. Long-term effects of this treatment await further observation.

#### References

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