Anti-Convulsion Effect of Botulinum Toxin A on Meige's Syndrome

Huang Heqing, Chen Kangning, Chen Li
(Department of Neurology, Southwest Hospital, Third Military Medical University of Chinese PLA, Chongqing 400038, China)
Luo Mingkui
(Staff Room of Mathematics, Third Military Medical University of Chinese PLA, Chongqing 400038, China)

Abstract

Background: Botulinum toxin A has been applied to treat muscular convulsion by local injection and shows obvious effects in reducing muscular hypertonia with fewer side effects.

Objective: To assess the effect of botulinum toxin A on Meige's syndrome concerning facial convulsion, therapeutic effect, and side effects.

Design: Randomized self-control clinical study.

Setting: Neurological Department of Southwest Hospital Affiliated to the Third Military Medical University of Chinese PLA.

Participant: Between June 2000 and May 2003, 24 outpatients were confirmed of having Meige's syndrome at the Neurological Department of Southwest Hospital, the Third Military Medical University of Chinese PLA and volunteered to receive botulinum toxin A (LANTOX) injection. Meige's syndrome was presented by convulsive eyelid closure in 10 cases, grinding teeth and smacking movement in 3 cases, involuntary blinking in 2 cases, frowning in 1 case, and mixed manifestations in 8 cases.

Method: Totally 24 patients with Meige's syndrome were subjected to LANTOX injection at multiple spots of convulsive muscles by dosage of 2.5-5 U in each spot. Improvement of facial convulsion and curative effects were assessed at least once by clinical examination or telephone follow-up. Convulsion was graded in four degrees according to Cohen's scaling standard. Curative effects: ① Complete alleviation: Convulsion was reduced to grade 0. ② Obvious alleviation: Convulsion dropped by more than two grades. ③ Partial alleviation: Convulsion dropped by one grade. ④ Ineffective: Convulsion was not attenuated.

Main Outcome Measure: ① Changes of muscular convulsion intensity after LANTOX injection in patients with Meige's syndrome; ② improvement of various symptoms after LANTOX injection; ③ side effects of LANTOX.

Result: Totally 24 patients entered the result analysis. ① Before treatment, there were

one case of grade 0-I, 7 cases of grade II, 10 cases of grade III and 6 cases of grade IV, as compared to 16, 6, 2 and 0 cases, respectively, after treatment (χ^2 = 95.489 4, P = 7.313 41 x 10^{-10}). ② LANTOX could alleviate eyelid convulsion in an average of 3 days, with curative effect reaching the peak in 2 weeks. Symptoms were found to be completely alleviated in 75% (18/24), obviously alleviated in 17% (4/24) and partially alleviated in 8% (2/24), with the total efficiency of 100%. The effective duration was 8-44 weeks with the average of 24.4 weeks. ③ Muscle weakness at the injected spot and incomplete muscular paralysis at the uninjected spot occurred for a short time after injection, but were alleviated automatically within 1-8 weeks.

Conclusion: LANTOX can obviously reduce convulsive degree and enhance the effects in treating Meige's syndrome; moreover, selection of muscles to be injected into and injection spots will help reduce side effects.

Introduction

Meige's syndrome, also known as blepharospasm-oromandibular dystonia syndrome, is a rare focal myodystonic disease. In order to make an objective evaluation and understanding of the curative effects on Meige's syndrome, we analyzed the treatment by focal injection of botulinum toxin A (LANTOX) on outpatients with Meige's syndrome in our hospital.

Subjects and Methods

Subjects

Between June 2000 and May 2003, 24 outpatients were confirmed of having Meige's syndrome at the Neurological Department of Southwest Hospital, the Third Military Medical University of Chinese PLA and volunteered to receive LANTOX injection. Inclusion criteria: ① All patients accorded with the clinical manifestations of Meige's syndrome (including blepharospasm and oromandibular dystonia syndrome). ② Follow-up by clinical examination or telephone call at least once. Exclusion criteria: Hemi-face muscular convulsion, tongue movement disorder, myasthenia gravis, eye-opening apraxia, and neurosis. Skull CT or MRI scanning confirmed brain atrophy in 9 cases, including 4 cases of multi-lacunar infarction at basal ganglion and 1 case of basal ganglion calcification. Nictation threshold was reduced with frequency increased in 5 patients upon nictation reflex inspection; meanwhile, the amplitude of R1 (reflecting single synaptic reflex) and R2 (reflecting multi-synaptic reflex) obviously increased, and even repeated inspection would not induce "adaptability". The subjects were 16 males and 8 females aged 37-73 years old with the mean age of 51.6 years; the course of disease varied from 1 to 48 months with the mean of 19.9 months. Four of them had received special medication (clonopin,

haloperidol, magnesium valproate, and tiapride), 15 of them had taken Chinese herbal medicine combined with acupuncture, but proved unsatisfactory. Meige's syndrome was presented by convulsive eyelid closure in 10 cases, grinding teeth and smacking movement in 3 cases, involuntary blinking in 2 cases, frowning in 1 case, and mixed manifestations in 8 cases.

Methods

LANTOX was produced by Lanzhou Institute of Biological Products affiliated to the Ministry of Public Health. It was diluted with normal saline to 5 U / mL before injected at the dosage of 0.05-0.1 mL (2.5-5 U) per spot [1]. The injection dosage was determined according to the principle of individualization, and injected spots were often the frontal muscle, orbicularis oculi, musculus zygomaticus major and minor, temporalis muscle, buccinator, masseter, levator labii superioris, and mentalis muscle. The severity of disease was assessed by telephone or clinical follow-up for at least once.

Standard of evaluation: Convulsion degree was graded referring to Cohen's scaling standard [2]. Convulsion was graded in four degrees. Curative effects: ① Complete alleviation: Convulsion was reduced to grade 0. ② Obvious alleviation: Convulsion dropped by more than 2 grades. ③ Partial alleviation: Convulsion dropped by one grade. ④ Ineffective: Convulsion was not attenuated.

Statistical analysis: Boundary distribution of inter-dependant paired dispersed data was subjected to uniformity test [3], SPSS10.0 software was used by the first and the fourth authors to carry out statistical process.

Results

Descriptive Statistics

Totally 24 cases were enrolled in this study. All of them completed the treatment and entered the result analysis with no loss.

Statistical Inference

Intensity changes of muscle spasms due to botulinum toxin A injection in patients with Meige's syndrome (Table 1).

Table 1 Changes of facial muscle spasms after botulinum toxin A injection in patients with Meige's syndrome (n = 24, n)

Time	Grading			
	0-I	II	III	IV
Before treatment	1	7	5	3
After treatment	16	6	2	0

$\chi^2 = 95.489\ 4$, $P = 7.313\ 41 \times 10^{-10}$ processed by dependant paired consistency χ^2-test.

Improvement of various symptoms of Meige's syndrome after LANTOX treatment

LANTOX began to exert effects within 1-7 days after injection with the average of (2.76 ± 1.87) days; the curative effect remained stable for 1-2 weeks, reached the peak at around 3-4 weeks, and lasted for 8-44 weeks with the average of (24.4 ± 10.9) weeks. The patients who received repeated injections were found to have obviously attenuated convulsion compared to after the first injection; moreover, the total dosage was slightly reduced although injection spots were unchanged.

Adverse events and side effects

LANTOX mainly included eyelid sagging, eye or mouth incomplete closure and diplopia. Eyelid sagging, which was observed in 5 cases, appeared 3-5 days after the injection and lasted for 3-6 weeks. Four cases with eye closure 4-7 days lasted for 2-8 weeks; 2 patients with mouth closure 4-7 days lasted for 1-7 weeks. Only 1 case of diplopia appeared at 9 days and continued for 2 weeks.

Discussion

In 1910, a syndrome firstly described by Henry Meige was mainly manifested as systematic and irregular contraction in orbicularis oculi muscle, frontal muscles and mouth, facial and tongue muscles, and afterward referred to as Meige's syndrome. The above manifestations commonly continue for several seconds to several minutes, and suddenly stop after 10-20 times of convulsive contractions and then reoccur within intervals of several seconds or minutes. This disease often cryptogenically attacks middle- and old-aged people, with the average onset age of 51.6 years in this study. In 1973, BTA was firstly applied by Scott [3] to treat squints; thereafter it began to be widely applied in the treatment of localized myotonia disorders [4]. BTA can act on nerve endings in a highly selective manner, entering into the target cells through receptor mediated cell blocking and suppressing the release of presynaptic acetylcholine, which results in muscular relaxation and paralysis [5]. Its mechanism for ineffectiveness is possibly due to nerve fiber sprout and vagus reconstruction.

The side effects are mainly presented by muscular weakness that occurs at the injection spot for a short time after injection (*e.g.* incomplete eye or mouth closure),

as well as partial muscular paralysis that appears at the uninjected spots (*e.g.* eyelid sagging and diplopia). We found that eyelid injection should be as close as possible to the inner and outer canthus; meanwhile, the upper and lower eyelids should be gently lifted. If the dosage is reduced by half and injection is slow during musculus orbiularis oris injection, the above side effects can be obviously reduced and recovery time can also be shortened. Side effects often alleviate automatically in 1-8 weeks, during which patients with incomplete eye closure should be given eye drops and eye ointment to avoid exposure keratitis. Gentle performance and patient hemostasis are required during the whole process, and no one has partial petechia or ecchymosis. It will be better to give injection under myoelectrographic (EMG) monitoring to effectively avoid side effects and promote the curative effects.

During the repeated injection process in 2 patients with Meige's syndrome (respectively for 2 and 3 times), effective duration was not found shortened. Drug resistance can be treated by continuous injection or increased dosage, or replaced by botulinum toxin B, or developing novel LANTOX containing less neurotoxic compound protein. In brief, LANTOX is convenient, safe and effective method to treat Meige's syndrome in order to avoid its common effect, and it is better to give injection under EMG monitoring.

References

1. Sun XM, Wu XL, Zhao HQ, Zhan SS, Zhang QY, Bao SY. Effects of botulinum toxin A on the dystonia by various dosage of injection. *Chinese Journal of Clinical Rehabilitation,* 2002; 6(18): 2701-2702.
2. Cohen DA, Savino PJ, Stern MB, Hurtig HI. Botulinum injection therapy for blepharospasm: a review and report of 75 patients. *Clinical Neuropharmacology,* 1986; 9(5): 412-429.
3. Scott AB. Botulinum treatment of strabismus following retinal detachment surgery. *Archives of Ophthalmology,* 1990; 108(4): 509-510.
4. Mu J, Wang YL, Xie P. Investigation and progress of myodystonia. *Chinese Journal of Clinical Rehabilitation,* 2005; 9(9): 141-142.
5. Manning KA, Evinger C, Sibony PA. Eyelid movements before and after botulinum therapy in patients will lid spasm. *Annals of Neurology,* 1990; 28(5): 653-660.

(Originally published in Chinese Journal of Clinical Rehabilitation, 2005; 9(37): 132-133)