A Clinical Observation on Treatment of Focal Dystonia with Botulinum Toxin A

Deng Zongguang, Chen Miliu, Huang Rong
(The Neurology Department of Sichuan Provincial Military Command Hospital, Chengdu 610041)

Key words: Botulinum toxin A; Focal dystonia; Injection site

The cause of focal dystonia is undefined. There is no satisfied treatment in the past. The effectiveness of oral medicine, acupuncture and moxibustion, thread burial therapy and surgery were not obvious. Since botulinum toxin A was approved by American FDA as a new medicine for clinical application in 1989, many papers reported the good results in the treatment of focal dystonia with botulinum toxin A in foreign countries [1]. In China, same results were reported by many hospitals, such as Neurology Department of Peking Union Medical College Hospital [2]. Botulinum toxin A, produced by Lanzhou Institute of Biological Products, was used in the treatment of blepharospasm, facial spasm, spasmodic torticollis, Meige's Syndrome, torsion spasm, myospasm caused by tetanus, masticatory spasm, writer's cramp and myotonia caused by motor neuron disease. The results were satisfied. Data of 67 cases were reported as follow.

Data and Method

1. Clinical Data

67 cases of focal dystonia were received by our clinic from May 1997 to April 1998. There were 46 cases of blepharospasm, 6 cases of facial spasm, 5 cases of Meige's Syndrome, 3 cases of spasmodic torticollis, 3 cases of torsion spasm, 1 case of myospasm caused by tetanus, 1 case of masticatory spasm, 1 case of writer's cramp, 1 case of myotonia caused by motor neuron disease. 36 male and 31 female, aged from 18 to 78 years old (mean: 43 years old). The course of disease were ranged from 3 months to 22 years; 8 cases were below 1 year, 11 cases were between 1 to 2 years, 29 cases were between 2 to 5 years, 13 cases were between 5 to 10 years, and 6 cases were above 10 years. Among 67 cases, 59 cases were treated by oral medicine, acupuncture and moxibustion, thread burial therapy and surgery before; however there were recurrences or no result. 1 case was treated by anhydrous alcohol block therapy before and recurred. Among 67 cases, 4 cases were caused by facial paralysis; 3 torsion spasm cases were caused by nuclear icterus and cerebral palsy, 1 myospasm case was caused by tetanus, 1 myotonia case was caused by motor neuron

disease, and 5 cases were caused by psychic factors. The causes of disease of 53 cases were unknown. Among all cases, the level of myospasm increased when patients are nervous.

2. Method

All cases histories and nervous system were checked and recorded in the clinic. 5 cases were checked by computed tomography, 2 cases were checked by magnetic resonance imaging, 8 cases were checked by electromyogram. All cases were injected with botulinum toxin A after diagnose. Those cases were followed up by phone or in clinic at 1 week, 2 weeks, 1 month and 6 months after injection.

Medicine: Lyophilized botulinum toxin A with two specifications, 40U and 100U, were produced by Lanzhou Institute of Biological Products and were stored in low temperature refrigerator. Before use, botulinum toxin A was reconstituted slowly by normal saline to a concentration 2.5 U per 0.1 ml. Multiple spots were injected with varied dosages laterally or bilaterally depend on the type and course of disease. Injection dosage was depended on the spasmodic level and range. According to our experience, the average starting dosage of each case should be 50-80 U. Injection dosage of each spot should be 2.5-5 U. Dosage higher than 500 U per session should be avoided.

Injection sites selection: Botulinum toxin A was injected selectively in the agonistic muscle or antagonistic muscle depending on the patients' condition, size and number of suffered muscles, and anatomic sites. Botulinum toxin A should be injected at a 2 cm interval and the injection sites and depth should be accurate. Injections at neck should not be too deep to prevent the diffusion of medicine and serious side effect. Staying in hospital is suggested to those serious spasmodic torticollis and torsion spasm patients. Patients will be allowed to go if there is no adverse reaction at 1 to 2 weeks after injection.

Efficacy assessment: Parameter of efficacy was accorded to Cohen and Albert spasmodic level [2]. Patients' feeling of improvement, changes of spasmodic frequency and intensity, and the off time were evaluated during the follow up.

Efficacy parameter: Improvement from Grade II-IV to Grade 0 is Total Relief; improvement from Grade II-IV to Grade I-II is Obviously Improved; improvement from Grade IV to Grade III is Partially Improved; no grade change is Ineffective.

Result

Conditions before injection were set as control. Follow up and assessment of spasmodic level were carried out after injection. Those data were analyzed by Ridit as follow (Table 1).

Table 1 Changes of spasmodic level before and after the focal dystonia treatment

Spasmodic level	Grade IV	Grade III	Grade II	Grade I	Grade 0	R ± SR
before Injection	11	41	12	3	0	0.50
1 week after injection	0	3	13	21	30	0.956 ± 0.264
2 weeks after injection	0	1	6	7	53	0.982 ± 0.264
1 month after injection	0	0	3	5	59	0.984 ± 0.264
6 months after injection	0	5	4	18	40	0.862 ± 0.264

R values of spasmodic level before injection and at 1 week, 2 weeks, 1 month and 6 months after injection were larger than 0.50 ($P < 0.05$). It shown that botulinum toxin A is obviously effective. As the R values are not changed between 1 week, 2 weeks, 1 month and 6 months after injection, it shown that botulinum toxin A treatment is stable in a short period. R value decrease at 6 months after injection; efficacy is reduced and some patients recurred.

At 1 week after injection, 56 cases (83.5%) show improvement. At 2 week after injection, 58 cases (86.5%) show Total Relief: 53 cases were improved from Grade II-IV to Grade 0, 14 cases were improved from Grade II-IV to Grade I-II. At 1 month after injection, 59 cases (88%) show Total Relief, 6 cases (8.9%) show Obviously improved, 2 cases (2.6%) show Partially improved. At 6 month after injection, 40 cases (59.7%) still show Total Relief, 6 cases (8.9%) were 2 grades less than that of before injection, 19 cases (28.3%) were 1 grade less than that of before injection, 2 cases (2.6%) recurred (spasmodic level were still lower that of before injection with 1 grade).

Treatment effect last for 26 ~ 34 weeks with average 30 weeks. One case used absolute alcohol block therapy after re-attack, and took this treatment, it was relieved obviously from Grade 3 (before treatment) decreased into Grade 2. After 26 weeks it was re-attacked and increased to Grade 3. The difference between before and after using other treatments of the patients is $P > 0.05$. After one week of treatment of rigidity of spasmodic torticollis, rotational spasm and motional neuron disease required supplemental injection, after two weeks showed obviously relief, after one month, two cases of spasmodic torticollis and two cases of rotational spasm were

completely relieved. One case of spasmodic torticollis and one cases of rotational spasm were partial relieved.

Twenty-two cases (32.8%) showed adverse effects; they were ptosis of labial angle, eye-lip ptosis, weakness of facial muscle, numbness of facial muscle and dry eye with pain, among them, one case showed difficulty of swallow. Adverse effects would be normally disappeared after four weeks; it would not last longer than six weeks.

Discussion

The major physiological changing of muscular spasmodic dystonia is the contraction of agonistic muscle and antagonistic muscle at the same time, it consist the un-control spasm at different position of patients. Botulinum toxin type A is a bacterial exotoxin generated from *Clostridium botulinum* during growth; it is a high molecular weight neurotoxin protein. According to different antigen, it divide as A, B, C, D, E, F and G7 types, among them, type A was developed since 1970 and applied in clinical study. In 1980, Scott [4] was the first one who injected this toxin into a volunteer and treated strabismus successfully. After that, this treatment method draws more and more neurologists' attention. Journals from foreign and China reported about treatment of neurological system dystonia by botulinum toxin type A become more and more. It is being one of the most important developments of neurological treatment. Botulinum toxin type A reacts on the pre-synaptic membrane, inhibits the release of acetylcholine, reduces the contraction of muscle and achieves the treatment prospect [6].

Author applied botulinum toxin type A to 67 cases of patient and follow up visit after treatment, efficiency was 100%, the total efficacy duration was longer than others reported in China, same as foreign reports [5]. There were three important points should be discussed; firstly, injection by professional operator, normal saline should be injected slowly into vial through the wall during reconstitution to prevent air bubble. If un-complete reconstitution occurs, it could chafe the vial bottom carefully on table upon complete reconstitution. Otherwise, the potency would be decreased due to the elongation of the botulinum toxin type A molecule by air bubble. Secondly, the injection dosage could not too low; the recommended dosage from Beijing Union Medical Hospital could be a reference [2], and a little bit lower than the dosage for Caucasoid is recommended. If the dosage is too low, the efficacy duration would be shorter, and induce antigen earlier and thus, effect on the efficacy of supplementary treatment. Thirdly, the accuracy of injection point selection, the separation of each injection point is about 2 cm; electromyography guidance could be used if necessary. For severe case, gentian violet could be used for allocation, fixed position by dilute

iodine, sterile and injection. Except normal injection points, intensive injection should be applied for severe case, it could achieve better treatment result and reduce adverse effect.

In this group, the re-attacked patient with absolute alcohol block therapy history showed the worst treatment effect, similar to the reports from national researcher [3], few of patients showed adverse effect and disappeared within 4 ~ 6 weeks spontaneously.

In conclusion, botulinum toxin type A manufactured in China with better treatment effect in the treatment of local dystonia, competitive price, safe and reliable, simple operation procedure, short treatment period, minimum painful feeling of patient, effective re-injection treatment, bright clinical application future. However, it should pay attention on the extreme case of adverse effect, for instant, difficulty of swallow and etc. Therefore, this treatment should be developed in well-condition hospital and guided under experienced doctors, botulinum toxin type A should be managed according to the regulation of anesthetic drug, in order to prevent any injury to patient by the unqualified doctor.

References

1. Schartz EJ, Johnson EA. Properties and use of botulinum toxin and other microbial neurotoxin in medicine. *Microbiol Review*, 1992; 56: 80.
2. Tang XF, Wan XH. Botulinum Toxin Type A in the Treatment of Local Dystonia and Facial Spasm. *Chinese Journal of Neurology*, 1996; 29: 111.
3. Wang WZ, Zhang LM. Clinical observation of botulinum toxin type A in the treatment of hemifacial and facial spasm. *Chinese Journal of Practical Internal Medicine,* 1997; 17: 674.
4. Scott AB. Botulinum toxin injection into extraocular muscles as an alternative to strabismus Surgery. *Ophthalmology*, 1980; 87: 1044.
5. Poungvarin N, Dvahastin V, Viriyavejakul A. Treatment of various movement disorders with botulinum A toxin injection: an experience of patients. *J Med Assoc Thai*, 1995; 78: 281.
6. Wang YC. Botulinum toxin and its clinical use. *Chin J Neuroimmunol Neurology*, 1996; 3(2): 124.

(Originally published in Medical Journal of National Defending Forces in Southwest China, 1999; 9(2): 83-85)