

Application of Botulinum Toxin A in Spastic Cerebral Palsy with Thumb Abnormality

*Liang Song, Wu Zhaofang, Han Wenling, Du Xiang, Jiang Kun, Liu Wenhua
(Rehabilitation Centre for Children with Cerebral Diseases, Zhongshan Hospital,
Wuhan, Hubei 430033, China)*

Abstract

Objective: To study the effects of botulinum toxin A (LANTOX) in spastic cerebral palsy (CP) with thumb abnormality.

Method: Fifty patients with CP were divided into two groups. The trial group was treated with LANTOX intramuscular injection and massotherapy, orthotics fixation, shangtian method training. The control group was treated with massotherapy, orthotics fixation, shangtian method training.

Result: After three month, the total effective rate of the two groups was respectively 96.0% and 78.0%. There was clear difference between the two groups. The trial group was better than the control group ($\chi^2=7.16$, $P<0.1$). And thumb range motion of the trial group was better than the control group.

Conclusion: It has positive effect that LANTOX intramuscular injection treat spastic CP with thumb abnormality.

Key words: Cerebral palsy; Thumb; Abnormalities; Botulinum toxins; Child

Spastic cerebral palsy (CP) with thumb abnormality affects patients' hand functions.

Patients with CP treated with LANTOX intramuscular injection were compared with patients treated only with shangtian method training, massotherapy and orthotics fixation in April, 2002. The results were shown as follows.

Information and method

1.1 Information

50 patients with CP were diagnosed and classified under the standard of the 1st National Seminar of Children with Cerebral Palsy. The age was in the range of 1 year and 5 months old to 8 years old. They were spastic and divided into two groups. 25 patients in the trial group included 17 males and 8 females. The mean age was 40.76 ± 20.63 months. 25 patients in the control group included 15 males and 10 females. The mean age was 47.04 ± 21.23 months. With statistical analysis, there was no significant difference in age between the two groups ($t=1.56$, $P>0.05$). There was no statistical meaning in the differences of age, type and pre-injection ROM.

1.2 Method

Under the foundation of upper limb rehabilitation training of shangtian method training, the control group was treated with massotherapy and orthotics fixation while the trial group was treated with LANTOX intramuscular injection.

1.2.1 Shangtian method

The upper limb method consisted of three phases. The hands kept on bending for 3 minutes. Bending and stretching interchanged for 15-20 times. Bending was held for 3 minutes at 2 times every day. Patients then took a rest of 15d after 20 times. There were 90d in total.

1.2.2 Massotherapy and orthotics fixation

Thenar eminence of children with CP was wiped. The thumb abducted outward. The motion persisted for 20-30 times. Pushed at Shen zhi and pressed at He gu. Patient's thumb was pulled and luffed by stretching and palpation. The thumb was sprung and twisted for a few times in the frequency of 15-20min/time at 1 time/d. 15 days of rest was given every 20 times. After massage, the thumb was fixed with thumb orthotics. The fixation was held for 20 h/d. There were 90 d in total.

1.2.3 LANTOX intramuscular injection

Reported by Koman^[2] and Sanchaz^[3], the dosage of LANTOX manufactured by Lanzhou Institute of Biological Production was 2.5IU (0.25ml) for 3-year-old children and 5 IU (0.5ml) for children older than 3 years old. Opponens pollicis muscle and adductor pollicis muscle were chosen. The patients were injected at the neuromuscular junction with 1 ml sterilized syringe.

1.3 Evaluation standard

It was evaluated by PROM and ROM^[4]. ROM of the two groups before and after injection was evaluated. By the standard of PROM, mild and remarkable improvements were classified as level 1 and 2 respectively.

1.4 Statistical analysis

It was represented as mean \pm standard difference ($x \pm s$). χ^2 test and t test were used to compare the two groups. The statistical difference was $P < 0.05$.

Result

2.1 Comparison of overall efficacy between the two groups

After therapy of three months, the efficacy of the trial and the control group was 96.0% and 78.0% respectively. There was a significant difference between the two

groups ($\chi^2 = 7.16$, $P < 0.01$). The therapeutic effect on the trial group was better than that on the control group. See Table 1.

Table 1 Comparison of efficacy between control and trial group

Group	n(Number of hands)	Therapeutic efficacy			Overall efficacy (%)
		Remarkable	Mild	Invalid	
Control	50	12	27	11	78.0
Trial	50	23	25	2	96.0

Note: Compared with the control group, $\chi^2 = 7.16$, $P < 0.01$

2.2 Comparison of ROM

From Table 2, the ROM comparison of both groups improved after therapy ($P < 0.01$). There was a significant difference between the ROM of the two groups ($t = 5.20$, $P < 0.01$). The degree of abduction of thumb in trial group improved remarkably compared to the control group.

Table 2 Comparison of ROM before and after injection ($\bar{x} \pm s$)

Group	n	Pre-injection ROM	Post-injection ROM
Control	50	21.82 \pm 6.40	33.30 \pm 8.56*
Trial	50	19.88 \pm 6.06	41.88 \pm 7.91**
t value		1.56	5.20
p value		>0.05	<0.01

Note: Compared with the measurement before injection, * $t = 13.07$, $P < 0.01$; ** $t = 23.24$, $P < 0.01$

2.3 Observation after injection of LANTOX in trial group

There were few side effects after injection of LANTOX. Transient pain at the injection sites occurred on 11 hands in 7 patients. From parents' report and clinical observation, LANTOX came into effect on 27, 13 and 8 hands at 72 hours, 1 week and 2 weeks after injection respectively. Limb dystonia remarkably improved in most of the patients. It came into effect in 9, 12 and 21 hands at 4, 8 and 12 weeks after injection.

Discussion

Damage of pyramidal tract causes flexion disturbance of upper limbs. Paralysis of adductor in thumb is more severe than that of abductor. This results in spastic cerebral palsy with thumb abnormality. Thumb shows an abnormal motion when extending outward the palm. Correction of thumb adduction at the early stage can prevent the abnormal motion and improve the overall function of the upper limbs.

The shangtian method is based on the Myklebust's theory in which the normal tendon function of human depends on the normal activities of opposite nervous excitation network. When nerve excitation causes contraction of agonistic muscle, relaxation of the corresponding antagonistic muscle will occur at the same time. If the brain is damaged, the network of the spine cannot perform its normal physiological function. This results in the contraction of both agonistic muscle and antagonistic muscle. In order to minimize dystonia, relieve spasm, correct abnormal posture, increase degree of joint motion, a series of techniques which suppresses the abnormal return of signal were used in the clinical rehabilitation training for the children with cerebral palsy (CP).

Massotherapy stimulates muscle and nervous system instantly. It helps to resume the elasticity of muscle, improve the mobility and stability of bones and joints. The therapy improves the function of the channels and adjusts humoral regulation. Deformation of limbs can be prevented.

Through regulation of abnormal activities of carpometacarpal joint of thumb, stabilization of joints, facilitation of abduction of thumb, suppression of adduction, and prevention in deformation of thumb and atrophy of thenar eminence due to unbalanced myodynamic. These methods can relieve thumb deformity and improve upper limb function. It is not very effective in patients in severe spastic cerebral palsy with thumb abnormality.

LANTOX is a highly molecular exotoxin produced during the cultivation of *Clostridium botulinum*. The chain of LANTOX binds to the presynaptic membrane of the cholinergic nerve instantly and inhibition of the release of acetylcholine is resulted. Prolonged muscle relaxation is enhanced and muscular spasm is then relieved^[5, 6]. The clinical trial of intramuscular injection of LANTOX was proved to be effective in the past 10 years^[7]. In the past 4 years, the application of LANTOX intramuscular injection in conjunction to rehabilitation training was proved to be a safe, effective and non-invasive method. The recommended dosage was 2-3 IU/kg at minimus every time. Spastic muscle which causes deformation should be chosen as the site of injection. The effect of LANTOX peaked at around 2 weeks after injection and persisted for more than 3-6 months^[2]. The time interval for repeated injection should be more than 3 months. With the conjunction to orthotics fixation and rehabilitation training, LANTOX intramuscular injection can give a better result to the therapy^[8].

Conclusion

There was a significant difference between the trial and control group in application of botulinum toxin A in spastic cerebral palsy with thumb abnormality after 3-month therapy. The dystonia of adductor of thumb significantly decreased. When the abductor was held in static state, the deformation of abductor vanished. Both the function and the appearance of upper limbs improved significantly. The improvement in functions and positions were consistent with denervation. Moreover, the study found that the duration of denervation was more than 9 months which was much longer than the effective period of the toxin. After recovery from muscle spasm, there was still induction of muscle size in the help of orthotics fixation.

In the study, there were 25 patients with 50 hands. Only 2 hands did not get the expected therapeutic result. LANTOX came into effect in 23 hands significantly and did not show any side effects. The toxin came into effect at 72 hours after injection in 27 hands. It showed effectiveness in 48 hands within 2 weeks after injection. Dystonia in the 48 hands decreased significantly at 12 weeks after injection. Only 7 patients had transient pain at the sites of injection and the pain relieved gradually. Report showed that patients felt swollen, painful and weak transiently and had other side effects like hypothermia^[9, 10]. Through massotherapy and orthotics fixation, it was more effective in treating spastic cerebral palsy with thumb abnormality. However, the therapeutic efficacy was lower in older and severe patients. LANTOX intramuscular injection is effective in relieving muscular spasm, correcting deformation and improving mobility. It is a safe and non-invasive method to treat spastic CP with thumb abnormality.

Reference

1. Lin Q. Summary of national meeting of spastic cerebral palsy in children. *Chinese Journal of Pediatrics*, 2989; 27(3):162-4.
2. Koman LA, Mooney JF, Smith B, *et al.* Management of cerebral palsy with botulinum-A toxin: Preliminary investigation. *Journ Pediatr Orthop*, 1993; 13(4):489-95.
3. Sanchez-Carpintero R, Narbona J. Botulinum toxin in spastic infantile cerebral palsy results in 27 cases during one year. *Rev Neurol*, 1997; 25(140):531-5.
4. Medical Division, Ministry of Health. Chinese Journal of Rehabilitation Medicine. Book 1. 1st ed. Huaxia Publishing Company Limited; 1999:29-59.
5. Wang YC. Botulinum toxin and its clinical application. *Chinese Journal of Neuroimmunology and Neurolog*, 1996; 3(2):124-7.
6. Li SC. Spastic Cerebral Palsy. 1st ed. Henan Science and Technology Publishing House; 2000:165-6.
7. Baker R, Jasinski M, Maciag-Tymecka I, *et al.* Botulinum toxin treatment of spasticity in

diplegic cerebral palsy: a randomized, double-blind, place-bo-controlled, does-tanging study. *Dev Med Child Neurol*, 2002; 44:666-75.

8. Wong U. Use of botulinum toxin injection in 17 children with spastic cerebral palsy. *Pediatr-Neurol*, 1998; 18:124-31.
9. Denislic M. Botulinum toxin in the treatment of cerebral palsy. *Neurol Peditiatrics*, 1995; 26(5):249-252.
10. Li JS, Huang Zhou JB. Effect of botulinum toxin in improving spastic cerebral palsy and its mobility function. *Journal of Clinical Rehabilitative*, 2002; 6(5):654-655.