Analysis on the Efficacy of the Botulinum Toxin Type A Treatment on Spastic Cerebral Palsy

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Spastic cerebral palsy, a common type of cerebral palsy, contributes to around 60-70% of children with cerebral palsy [1]. The current spasm-relieving treatment includes surgical operation, oral drug for muscles relaxation, nerve blockade and intrathecal injection of Baclofen, etc, in which the nerve blocking treatment is the most popular. Recently, the application of botulinum toxin type A (Lantox) was developed as a nerve paralyzer.

Lantox was used in the nerve blockade from year 2000 in our hospital, and the experience we gained was mentioned as follows.

Information and Method

During June 2000 to September 2002, 38 cases of cerebral palsy children were treated in our hospital. According to the standard in the first National Cerebral Palsy Conference [2], all these cases were diagnosed as spastic cerebral palsy. The 24 males and 14 females aged from 2 to 15 (average 6.2 ± 2.6). Among them, 26 cases were outpatients and the remaining 12 cases were inpatients. The 38 cases, 17 cases were diplegia, 9 cases were double diplegia, 7 cases were hemiplegia, 4 cases were quadriplegia and 1 case was monoplegia.

The Lantox dry powder used was made in Lanzhou (stored under -20 to -5 ℃ in dark, and immediately used after the dilution with normal saline to 50 IU/ml), the single use nerve blocking insulating injection needles were made in Japan, conducting cream, surface electrode, conducting wire and stimulator were made in Shanghai within the therapeutic instrument with model number G680522A (continuous wave, impulse frequency 2. 667～83. 333 Hz ,current 0～6 mA ,voltage 6 V)

1. Positioning: According the anatomy, the projection of the selected muscles on the surface was confirmed, and tape was used to fix the stimulator on the surface of the contralateral antagonistic muscles, the impulse frequency was 3-5 Hz and the current was temporary fixed at 3mA. Then the cathode of the stimulator was used to

find the target around the projection area, with the current continuously adjusted. When the minimal current can trigger the largest contraction of the corresponding muscle, the blocking point was found and gentian violet was used for marking.

2. Blockade: Regular disinfection was done on the skin surface, applying 0.5mA current with constant impulse frequency, the insulating injection needle was connected to the cathode of the stimulator. Through the blocking point, the needle pierced into the subcutaneous tissue. By adjusting the depth of the inserted needle and current, the drug was injected when the largest muscles contraction was triggered by the minimal current.

3. Muscles Selection and Drug Dosage: Select calf muscles, Soleus muscle, Tibialis posterior muscle and adductor muscles groups (including Adductor longus muscle, Adductor brevis muscle, Adductor magnus muscle, Gracilis muscle and pectineal muscle). In this study, 61 injections were done in the calf muscles or soleus muscle, 6 injections were done in Tibialis posterior muscle and 1 injection was done in the pectineal muscle. The dosage was determined according to the muscle tone and the weight of the patient. According to the modified Ashworth scale [3], if the muscle tone is in grade 1-2, the Lantox injection dosage will be 2-4 U/kg; if the muscle tone is in grade 3-4, the Lantox injection dosage will be 4-6 U/kg. The muscles shape and size determine the number of sites for injection. There are commonly 2-3 injection sites for Soleus muscle, Tibialis posterior muscle and adductor muscles groups and 4-6 injection sites for the calf muscles. The Lantox injection dosage was 55-150 U each time (average 80.4 ± 21.4 U), the injection dosage was 10-80U for each piece of muscles.

The level of spasticity was assessed by modified Ashworth scale. Assessments on the muscle tone of the treated muscles and movement ability were done before blocking, 0 hour, 6 hours, 12 hours and 24 hours after blocking treatment. Moreover, daily assessments at fixed times will be done and recorded in the following 10 days. The conditions will be observed and recorded weekly after 10 days.
Standard of efficacy assessment: Very effective – the level of spasticity reduced and the movement ability improved; effective – the level of spasticity reduced but no obvious improvement in the movement ability ; ineffective – no reduction in the level of spasticity with no obvious improvement in the movement ability. The matching t-test was used for statistical analysis.

Result

47 man-times, 15 man-times and 6 man-times had their treatments very effective, effective and ineffective respectively. The effective rate is 91.2% and the rate of very effective is 58.8%. The average of Ashworth score was 2.43 ± 0.63 and 1.40 ± 0.76 before and after the blocking treatment respectively. After the matching *t*-test, the result, $p<0.01$, indicated that the degree of spasticity decreased.

The onset time for the Lantox injection was between 12 hours to 8 days (average 4 ± 1.8 days), the effect of the treatment lasted for 8 to 51 weeks (average 23.9 ± 6.2 weeks).

In the 38 cases, 3 cases had their injection sites painful after the injections. Muscle weakness was found in one case, the patient is thus tumbled over easily. The side effect occurred at the incidence of 5.8%. All the adverse events disappear spontaneously without special treatment.

Discussion

Spasm is the key factor for the retarding growth and abnormal movement posture in cerebral palsy patients. The mechanism is complex; it is generally agreed that due to the damage in the central nervous system, the control of spinal cord stretch reflex by the upper centre is retarded or abnormal, resulted in spasm by overreacting or hypersensitive stretch reflex. However, it should be noted that spasm caused by cerebral palsy does not affect all the muscles, usually the muscle tone of individual muscles increased while the muscle tone of the other muscles remain normal [4].

Lantox originally comes from a single polypeptide chain, it is then activated by selective hydrolysis at specific location, in which it is decomposed into one heavy chain and one light chain. The hydroxyl terminal of the heavy chain can attach to the receptors present in the postsynaptic end of the cholinergic nerve terminal, while the amino terminal producing a channel for the passage of light chain into the cell. Through the enzymatic reaction of the light chain, the release of the vesicles containing acetylcholine is inhibited, and the decrease in the strength of muscles contraction will then result in a reduction of muscle tone. [5]

The effect of the Lantox nerve blocking treatment lasted for relatively long time, 5 months in average. This allowed the treated children to learn the correct movement and posture in the rehabilitation training when their spasticities were temporary relieved. By that, the image of correct movement pattern could be formed in there

cerebrum and thus provide room for further develop and growth in movement. Therefore, even if the treatments became no long effective after 5 months, the children had already grasped the pattern of correct movement, and their ability in movement would not be worsen.

The side effects of Lantox were pain at the injection site, muscles weakness and allergy etc [6]. But these events were generally mild and require no special treatments. In this study about the nerve blocking treatment, pain at the injection sites and muscles weakness were found in the patients , but they were recovered spontaneously. After deliberation, we believed that the pain was related to the damage of muscles and blood vessels after injection, and the muscles weakness was related to the over dosage of Lantox.

To conclude, Lantox nerve blockade is a fast-acting, highly selective, simple, cheap and reliable treatment for spastic cerebral palsy. Moreover, as it causes only few side effects, the prospect of Lantox injection is promising in China.

References

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(Originally published in the Chinese Journal of Physical Medicine and Rehabilitation, 2004; 26(1): 49-50)