Clinical Study of Botulinum Toxin Type A in the Treatment of Lower Limb Spasticity after Stroke and Head Injury

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Abstract

Objective: To determine whether botulinum toxin (LANTOX) is an effective and safe treatment for lower limb spasticity and improve walking ability after stroke or traumatic brain injury.

Method: 27 cases with stroke or traumatic brain injury affecting the muscles of lower extremity were selected to receive local intramuscular injection. The injected dose is between 50-100IU/muscle. All patients received rehabilitation therapy that focused on walking training. Patients were assessed at entry, and 2, 4 weeks post-treatment. The muscle tone was assessed by the modified Ashworth Scale. The changes of time-distance parameters were measured by footprint gait analysis. The correlation relationship between muscle tone and gait parameters was analyzed.

Result: Compared to pretreatment values, the total muscles spasticity, walking distance, and speed were significantly improved in all groups respectively, decrease in the modified Ashworth Score ($P<0.05$), and increase in the time-distance parameters except step angle ($P<0.001$) were achieved. Compared preinjection with 4 weeks postinjection, step length, step width , step speed have significant difference ($P<0.05$), compared 2 weeks with 4 weeks postinjection, step length, step speed have significant difference ($P<0.05$), but step width and angle have only little changes. The correlation analysis shown there is a good relationship between muscles tone decrease and step length ($r=0.650$ to -0.875). No significant side effects were seen.

Conclusion: The results of the present study indicate that botulinum toxin type A injection combined with rehabilitation therapy resulted in a long-lasting decrease in spasticity and an improvement in gait after stoke or traumatic brain injury. The combination of focal chemodenervation with rehabilitation procedures enables better improvement for specific functions.

Key words: Stroke; Traumatic brain injury; Muscle tone; Botulinum Toxin A; Rehabilitative therapy

Botulinum Toxin Type A is effective to treat small muscle spasm in the field of ophthalmology and neurology. It is also effective to treat large muscle spasm caused by brain injury, for example, stroke, brain trauma and cerebral palsy. There is more

report for upper limb spasm than that of lower limb spasm and the majority is related to cerebral palsy. From Aug 1999 to Dec 2000, 27 cases of stroke and brain trauma patients who developed walking problem were received LANTOX injection on target muscle. With combination of gait training, the efficacy and safety of LANTOX to treat lower limb spasm for the improvement of muscle movement and walking ability was investigated.

Method

1. Clinical Information

27 patients who had suffered from stroke and brain trauma were stayed at hospital. 9 cases had brain trauma and 18 cases stroke. 15 were male and 12 were female, age from 18 to 70 (average 58.3±12.8). 10 cases were right side palsy and 17 cases were left. Average medical history was 2.5 months. The selection criteria for this study were: 1. The patient could walk independently or helped with stick but showed spasm of gastrocnemius muscle which caused extensive stretch or flection of knee or hip joints, heel cannot touch the ground or circular gait. 2. Patients could walk more than ten meters with stick. 3. Antispasmodic drug treatment was unsatisfactory and with many side effects or cannot keep the course of medication.

2. Injection Method

According to the condition of spasm, the lower limb muscle including hip adductor muscles (great adductor muscle, long adductor muscle and short adductor muscle), hamstring muscles (semitendinous muscle, semimembranous muscle and biceps), gastrocemius muscle and rectus femoris muscle were selected for injection. Three to five muscles were injected with LANTOX (Lanzhou Institute of Biological Products, Health department) each time for each patient. 2ml 0.9% sterilized physiological saline was used for reconstitution. 5 IU/0.1ml concentration was achieved and then stand for 5 minutes. After completely dissolved without bubbles, 1ml skin test syringe and no.6 needle was used for injection in a suitable skin depth. The patient was place and kept in a suitable position. After skin disinfection, the target muscles were injected. The injection locations were mainly in the center of abdomen. The location was confirmed by touching at the harder muscle after sterilized glove was wear. According to the muscle size, extent of spasm, each point had 5-10 IU injected. The total dosage in each muscle was 50-100 IU referring to recommend dosage. Injection dosage was $\leq$ 400 IU for each patient each time. Rehabilitative therapy like gait training was performed as usual after injection.

3. Evaluation Criteria

The efficacy was evaluated according to follow criteria at the time before injection, two and four week after injection:

1.1 Muscle tone

Modified Ashworth Scale, MAS was used to evaluation muscle spasticity.

1.2 Gait analysis

Footprint analysis method was used to measure and record the walking time and distance parameters. The patient was required to walk ten meters walkway independently or with stick. The step length, step width, step angle and walking speed at the spasmodic side was measured and recorded. Average value was calculated after three times of performance.

4. Statistical Analysis

Friedman method and Spearman scale was used for the measurement of change of muscle tone and gait parameters. SPSS 8.0 was used for statistical processing, the limit for significant difference was 0.05.

Results

According to the opinion of patients and their family members, the spasmodic muscles were softened, pain reduced, extent of movement of joint increased, duration of retraction increased. The movement of lower limbs was improved. The width of foot and shoulder was equal and improvement of knee extension and flection when stand was observed. Circular and scissor gait during walking were improved with heel could touch the ground. Comparing the muscle tone before and after injection of LANTOX, the muscle tone had obvious improvement. After two weeks of injection, except rectus femoris muscle, other muscles had obvious decrease of muscle tone ($P<0.05$). There was significance difference ($P<0.05$) of muscle tone comparing before and four weeks after injection. When compared with the result of two weeks after injection, the muscle tone had no significant change ($P>0.05$), no increase or decrease. Comparison of the gait, time and distance parameters (T-D value) (Table 2), they had different extend of improvement ($P>0.001$ or <0.005) except walking angle parameter. There was significant difference ($P<0.05$) when comparing step length, step width, walking speed before and four weeks after injection. Compared the result of two and four weeks after injection, there was improvement of step length and walking speed ($P<0.05$) but no change in step angle.

Table 1 Ashworth scores measured in tone of different muscle group before and after LANTOX injection (Mean ± s)

Target muscle	N	Before Injection	After two weeks	After four weeks	X^2	P
Hip adductors	13	2.30±0.63[1]	1.15±0.89[2]	0.92±0.64[3]	20.36	<0.001
Hamstrings	8	2.63±0.74[1]	1.63±0.92[2]	1.00±0.76[3]	14.21	<0.01
Gastrocnemius	17	2.65±0.61[1]	1.53±0.72[2]	1.06±0.83[3]	29.71	<0.001
Rectus femoris	12	2.17±0.72[1]	1.75±0.45[4]	1.17±0.39[3]	14.80	<0.01

[1]Compared before injection with after four weeks, P<0.05

[2]Compared before injection with after two weeks, P<0.05

[3]Compared after two week with after four weeks, P>0.05

[4]Compared before injection with after two weeks, P>0.05

Table 2 Gait changes of 27 cases in T-D values before and after LANTOX injection (Mean ± s)

T-D value	Before injection	After two weeks	After four weeks	X^2	P
Step length (cm)	33.93±11.42[1]	39.48±8.99[2]	42.89±7.29[3]	44.82	<0.001
Step width (cm)	9.29±3.18[1]	10.48±1.76[4]	10.37±1.08[5]	6.02	<0.05
Step angle (degree)	8.89±4.31[6]	9.52±1.58[4]	9.81±1.21[5]	3.31	>0.05
Walking velocity (cm/s)	32.11±9.01[1]	38.52±6.67[2]	44.59±5.13[3]	51.02	<0.001

[1]Compared before injection with after four weeks, P<0.05

[2]Compared before injection with after two weeks, P<0.05

[3]Compared after two week with after four weeks, P>0.05

[4]Compared before injection with after two weeks, P>0.05

[5]Compared after two weeks with after four weeks, P>0.05

[6]Compared before injection with after four weeks, P>0.05

Spearman scale analysis revealed that the decrease of muscle tone of hip adductor muscles, hamstring muscles, gastrocnemius muscle and rectus femoris muscle had different extent of relationship with step length. Hamstring muscle and step length had negative relationship (r= -0.752 to -0.875, P<0.05 or P<0.01). Furthermore, different muscle had different biased towards step angle, walking velocity, step width. Rectus femoris muscle had negative relationship with walking velocity (r=-0.621 to -0.900, P<0.01). There was positive relationship between hip adductor muscles and step angel (r=0.564, P<0.05). Gastrocnemius muscle was also positive related to step

width ($r=0.524$, $P<0.05$).

Discussion

Recently used anti-spasmodic drug could be divided into two main types: oral drug and local drug. Treatment of target muscle or spasmodic muscle by local injection could had the effect concentrated on target muscle and reduced general side effect. This could improve a particular muscle function, reduce pain and spasm. The drug commonly use was Botulinum Toxin Type A. It is a potent muscle relaxant and caused muscle paralysis after injection. The toxin molecules combined with the receptors of acetylcholine vesicles at the neuromuscular junction and inhibited the released of acetylcholine from the presynaptic nerve, so as to reduce muscle spasm. Many clinical reports reported the good result of LANTOX for treatment of hemifacial spasm and blespharospasm. Although large muscle was controlled by many nerves, this clinical study and efficacy evaluation revealed that local injection of LANTOX could effectively treat lower limb large target muscle spasm and showed gait improvement. The result was identical to clinical study of other countries. For table 1, the spasm condition of the target muscle had greatly improved. In 13 cases, the Modified Ashworth Score was decreased from 2.30 ± 0.63 to 1.15 ± 0.89 in the time of two weeks after injection of hip adductor muscle. There was significant difference of muscle tone and had more improvement four weeks after injection. Except one case had lower fever after injection, there was no any side effect. This proved that LANTOX was a safe and effective treatment method for local muscle spasm.

After brain injury, most patients had the problem of palsy and they wanted to be able to walk. However, walking required three elements which were weight bearing, movement and balance. These relied on the proper activation of muscle, especially muscles of lower limb. Long period spasm of lower limb muscle after brain injury could cause muscle shrinkage, hardening of joint, decrease in muscle activation which effected gait. Other than observation, change of gait could also be diagnosed by step analysis method by measuring step length, width, angle and walking velocity parameters. They revealed the walking ability and velocity affected by palsy. In table 2, injection of LANTOX into target muscle with the combination of gait training, the spasmodic condition and muscle tone of each muscle were reduced in two weeks after injection. The step length increase from 33.93 ± 11.42cm to 39.48 ± 8.99cm and reached 42.89 ± 7.29cm in four weeks' time. There was significant difference after tested by Friedman method ($P>0.001$). There was also improvement of walking velocity ($P>0.001$). Compared with before injection, although significant difference occurred after 4 weeks after injection for the step width, it still had improvement

throughout the period. This was consistent with the report of Hyman N which showed the distance between the knees increased after injection of Dysport into hip adductor muscles.

The analysis of result proved that there was close relationship between the decrease of muscle tone and the change of gait parameters. Except step length, different muscle had different biased towards step angle, walking velocity and this was consistent with the role of different muscle during the gait period. In the analysis of three dimensional gait, in the course of walk and stand of a normal person, heel touched the ground first and then the toes lifted from the ground. The gastrocemius muscle contract centrifugally and then centripetally which worked antagonistically with strengthen of the back and then forwarded the tibia. The spasm of gastrocnemius muscle caused the bending of metatarsus which indirectly affected step width. In the course of swinging (acceleration period to mid period of swing to deceleration period), rectus femoris muscle, hip adductor muscles, hamstring muscles were involved in the control of flection of hip, knee and ground touching alternatively. The rectus femoris muscle kept the stretch of knee by contracting centripetally and then centrifugally to work antagonistically with knee flection and to control the bending degree. Spasm of rectus femoris resulted in too much knee stretch or circulating gait which affecting the walking velocity. Spasm of hamstring muscle caused knee flection and difficulty of moving forward which affecting the step length. Spasm of hip adductor muscle caused scissor gait and affecting step angle and step width. Actually, at different period of walking, the lower limb muscle worked synergistically to achieve normal gait and walking motion. The relationship of parameters of gait and different muscles still required further investigation.

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