

Color Doppler ultrasound-guided botulinum toxin type A injection combined with an ankle foot brace for treating lower limb spasticity after a stroke

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Abstract. – OBJECTIVE: To explore the effectiveness of the color Doppler ultrasound-guided botulinum toxin type A (BTX-A) injection combined with an ankle foot brace (AFO) for treating lower limb spasticity after a stroke.

PATIENTS AND METHODS: A total of 103 post-stroke patients with lower limb spasticity were divided into three groups: the control group treated with conventional therapy and rehabilitation training, the observation group treated with conventional therapy, rehabilitation training and botulinum toxin type A injection, the treatment group treated with AFO plus the same treatment received by the observation group. The muscle spasms were evaluated using the Clinic Spasticity Influx (CSI), movement with the Fugl-Meyer Assessment (FMA), dynamic and static balance with the Berg Balance Scale (BBS), and daily life activities with the Functional Independence Measure (FIM), respectively.

RESULTS: Compared the first month after treatment with the prior treatment, there were significant differences in CSI, FMA and FIM scores in both control group and the observation group ($p < 0.05$). However, no differences were noticed in the control group ($p > 0.05$). Compared the third and sixth month after treatment with prior treatment, there were significant differences in these three groups ($p < 0.05$). In terms of treatment time, the BBS scores were always higher in all three groups after one month, three months and six months treatment than prior treatment ($p < 0.05$), and there were significant differences in third month and sixth month after treatment compared with the first month treatment ($p < 0.05$). Compared the third month after treatment with the sixth month, there were significant differences in all three groups ($p < 0.05$).

CONCLUSIONS: The color Doppler ultrasound-guided BTX-A injection combined with AFO can effectively promote patients with post-stroke lower limb spasticity in lower limb muscle spasm, movement, balance and daily life activities.

Key Words:

Color Doppler ultrasound, Botulinum toxin type A, Lower limb, Spasticity, Ankle foot brace, Stroke.

Introduction

Approximately 80-90% of stroke patients with hemiplegia have varying degrees of increased muscle tone¹, which causes foot drop and varus in the lower extremities. If untreated, it can lead to permanent high muscle tension, joint contractures and abnormal movement patterns of the affected limbs, resulting in the inability to sustain weight, balance or even walk. Looking for optimal spasm control measures has become a hot topic in the rehabilitation medical community. Sadly, systemic medication is ineffective and it can trigger adverse reactions. This study assesses the efficacy of botulinum toxin type A injections with an ankle joint foot orthotics in treating the lower limb with spasticity. The study focuses on the spasticity index, exercise and balance functionality. We hope to provides a basis for optimizing rehabilitation.

Patients and Methods

A total of 103 post-stroke patients with lower limb spasticity admitted to the department of neurology in our hospital from October 2006 to October 2012 were enrolled in this study. They were divided into three groups: control, observation, and treatment group according to a random sampling, regardless of sex, nature of lesion, hemiplegic side, age, duration of course and other factors ($p > 0.05$) (Table I).

Table 1. General information by group.

Group	Gender		Nature of lesion		Hemiplegia group		Age	Course of disease
	Men	Women	Infarct	Bleeding	Left	Right		
Control group	15	18	21	12	23	10	64.23 ± 12.38	15.35 ± 1.81
Observation group	16	19	23	12	21	14	62.76 ± 11.52	16.35 ± 1.22
Treatment group	18	17	24	11	23	12	63.42 ± 10.19	17.01 ± 1.07

The inclusion criteria were as follows: (1) First onset of stroke confirmed by computed tomography (CT) or magnetic resonance imaging (MRI) and referred to the diagnostic criteria for cerebral infarction and cerebral hemorrhage as per the Guidelines for Diagnosis of Cerebrovascular Diseases developed at the Fourth National Conference on Cerebrovascular Disease in 1995²; (2) Extensor spasm pattern of the lower limbs with spastic varus or foot drop not controlled with traditional physical therapy and medication; (3) Composite Spasticity Scale (CSS)³; score ≥ 10 ; and (4) Patients does not exceed 75 years with good cognitive function, agree to participate in the study and sign an informed consent before enrollment.

The exclusion criteria were as follows: (1) Severe cognitive dysfunction; (2) Older than 75 years; (3) Severe cardiopulmonary dysfunction; (4) Flexor spasm pattern of the lower limbs; (5) Complications of rheumatoid arthritis, fractures, joint contractures, injury or infection of injection sites, or other diseases that affect limb functions; (6) Intake of drugs aggravating neuromuscular junction transmission disorder in the past week; (7) Experience of nerve injury or surgical treatment on the target limbs; (8) Presence of asthma or allergic reactions; and (9) Unwillingness to participate.

II Management

Dosage and method for BTX-A injection: BTX-A lyophilized powder produced by Lanzhou Institute of Biological Products, 100 u/ampule, was diluted with 4 ml 0.9% saline into 25 u/ml, fully dissolved until no foam generated. We draw BTX-A solution with 1 ml syringes. The depth of injection was determined by ultrasound, and the injection was made with an electrical stimulation needle.

The supine or prone position was used to place the ultrasound scanner depend on the target muscle. The muscle was pressed at the belly to iden-

tify the target site based on the contraction dynamic from passive movement by real-time ultrasound. If necessary, the assistant could pull back the target muscle along the long axis and induce clonus, spasms or increased muscle tone for further confirmation. Under real-time ultrasound, following a routine disinfection at the injection site, a dry cotton ball was used to wipe clean the disinfectant. A proper amount of coupling agent was applied to the ultrasonic probe, which was then coated with a sterile sleeve wrap. A water balloon was placed between the probe and the skin to determine the cross-sectional area and the depth of the target muscle, which allows us to calculate the estimated volume and determine the dose and the injection point. Under guidance of the color Doppler, the prepared BTX-A was injected into the target muscle where spasms were the most obvious (based on individual case). Stratified injection was used according to the thickness of the muscle. It is noteworthy that the site of injection should avoid blood vessels and nerves. The decision could be made according to lidocaine nerve block or limb functional status (such as when spasms were obvious when bending the knee), then gastrocnemius should be the primary target; and if extending, soleus should be primary. In case of deep peroneal nerve block, a flat foot was obviously better than tibial nerve block. The primary responsible muscle for strephenopodia should be tibialis anterior muscle, followed by the posterior muscle. There is certain flexibility in selecting the injection location and dose. After injection, patients were observed for any allergies and other adverse reactions.

Materials used were the following: electrical nerve stimulator and insulated needle produced by Jiangsu Suyun Company; Botulinum toxin injection ultrasound balloon: invented by Ding Xudong, Chen Huaxian and others, patent No. ZL201120341018.X. Ultrasound apparatus: Philips IU22 type.

We used the following orthotics for rehabilitation: Static or dynamic ankle foot brace produced by the Feiyue Company. The device was applied after BTX-A injection for three days in conjunction with conventional rehabilitation training. The control group was treated with the rehabilitation only, including Bobath concept, range of motion (ROM) training, walking, massage, physiotherapy and occupational therapy, activities of daily living (ADL) training, and so on. For the observation group, in addition to same the rehabilitation activities like the control group, BTX-A injections were administered. In the treatment group, patients received same treatment like the observation group along with an ankle foot brace. Then, if the lower limb function improved, the orthotics were changed from astatic to dynamic type to improve lower extremity separatist movement, walking and ADL training.

Statistical Analysis

SPSS 13.0 (SPSS Inc., Chicago, IL, USA) was used for data analysis. Variance analysis was used to compare the distribution in terms of sex, disease and hemiplegic side on three groups, and *t*-test or F-test was used to compare the CSI, FMA, BBS, and Modified Barthel Index (MBI) scores. *p* < 0.05 was considered statistically significant.

Results

Functional evaluation was conducted before treatment and in the first month, third month and sixth month after treatment in these three groups

using the CSI⁴, for tendon reflexes, muscle tone, and myoclonus. Results guidelines: 0-9 points: mild spasm; 10-12 points: moderate spasm; 13-16 points: severe spasm. The Fugl-Meyer Assessment (FMA)⁵, lower extremity motor score rating scale was used to evaluate the upper and lower limb flexion movement, reflection, coordination and movement velocity. The highest score was 34 points for the lower limbs, with the higher scores representing the better motor function. The BBS⁶ was used to evaluate the dynamic and static balance. The full score was 56 points, with the higher scores representing the better balance. The function independence scale⁷, was used to evaluate the lower limb disability, with the maximum score being 126 points (out of 91 points for the movement, and 35 points for the cognition category), the minimum being 18 points. 126 points = complete independence; 108-125 points = basic independence; 90-107 points = conditional independence or very mild dependence; 72-89 points = mild dependence; 54-71 points = moderate dependence; 36-53 minutes = severe dependence; 19-35 points = very severe dependence; 18 points = totally dependent.

The results were as follows:

1. There were no significant differences in CSI, FMA, FIM, and BBS scores in all these three groups compare with corresponding prior treatment (Table II).
2. There were significant differences in CSI, FMA and FIM scores both in the treatment and observation groups compare the first month treatment with pretreatment (*p* < 0.05). There was no difference noted in the control

Table II. CSI, FMA, FIM, and BBS index before and after treatment ($\bar{x} \pm s$).

Group		Before treatment	1 month after treatment	3 month after treatment	6 month after treatment
CSI	Control group	12.70 ± 1.54	9.07 ± 1.02	10.78 ± 1.64*	10.12 ± 1.56*
	Observation group	11.80 ± 1.76	8.05 ± 1.32*	9.10 ± 1.94*	9.20 ± 1.32*
	Treatment group	12.10 ± 1.91	7.44 ± 1.02*	7.87 ± 1.03* ^o	5.92 ± 1.12* ^o
BBS	Control group	30 ± 6.52	36.06 ± 6.82	39.11 ± 6.76*	40.21 ± 7.14*
	Observation group	30 ± 7.22	40.06 ± 7.01*	44.53 ± 6.81*	45.07 ± 8.04*
	Treatment group	30 ± 5.98	42.37 ± 5.67*	48.01 ± 7.04* ^o	49.25 ± 4.67* ^o
FMA	Control group	8.42 ± 2.42	8.97 ± 2.52	6.01 ± 1.59*	7.65 ± 1.07*
	Observation group	9.34 ± 1.37	12.29 ± 2.31*	14.52 ± 3.01*	17.61 ± 3.98*
	Treatment group	8.72 ± 1.45	13.78 ± 2.98*	16.72 ± 2.49* ^o	23 ± 2.221* ^o
FIM	Control group	45.7 ± 10.2	50.2 ± 11.3	54.3 ± 11.5*	60.3 ± 10.5*
	Observation group	47.6 ± 12.1	60.3 ± 11.7*	70.5 ± 10.4*	72.4 ± 10.8*
	Treatment group	47.1 ± 12.6	69.5 ± 12.1*	80.7 ± 12.3* ^o	100.2 ± 11.4* ^o

Note: **p* < 0.05 compared with before treatment; ^o*p* < 0.05 comparing the treatment group with control and observation groups.

group ($p > 0.05$). Both the third month and sixth month after treatment, there were significant differences compared with prior treatment in all three groups, and there were significant differences compared the third month with sixth month after treatment between any two of these three groups ($p < 0.05$). There was no significant difference between the observation and control groups ($p > 0.05$) (Table II).

3. BBS scores were always higher in all three groups in the first month, third month and sixth month after treatment than prior treatment ($p < 0.05$). There were significant differences compare the third month and sixth month with the first month after treatment in all three groups ($p < 0.05$). Compare the third month after treatment with sixth month after treatment, there were significant differences between any two of these three groups ($p < 0.05$) (Table II).

Discussion

During the rehabilitation period, recovery of hemiplegic limbs is based on establishing free and normal movement patterns⁸. Spasm can affect free movement. It is the key to movement recovery. Spastic varus and foot drop affects the standing and gait, resulting in the patient's ankle contractures and Achilles tendon shortening, making it difficult for the patients to wear foot orthotics. Hence, spasms should be relieved as early as possible.

Botulinum toxin type A is a toxin produced by the bacterium *Clostridium botulinum*. It acts on the peripheral cholinergic nerve endings to inhibit the quantum release of acetylcholine weakening muscle contraction. It can be used to re-establish the strength and balance between the agonist and antagonistic muscles, relieve cramps, regulate posture, and enhance motor functions^{9,10}. The muscle relaxation effect can last for a week after injection BTX-A. Most patients experience their peak improvement in sixth weeks after injection, and efficacy will last for about 12 weeks¹¹.

By the ultrasound imaging, the accuracy of injection can be increased. Needle insertion guided by ultrasound into the target muscle is very intuitive, clear, painless and non-invasive, and it is useful to locate deep smaller muscles by this guide. Auxiliary electrical stimulation needle can be used to stimulate target muscle contraction, which increases the accuracy when locating the

target muscle. The balloon close to the skin, increasing the ultrasonic acoustic window and effect, thus avoiding impact of air on the image quality.

All patients within the three groups had a stroke six months ago. The CSI scores indicates that the patient's limb muscle tone is increased before treatment. From the treatment results, there were no significant differences between the first month treatment and prior-treatment in the control group ($p > 0.05$). Improvements in CSI scores were noted in the observation group and treatment group, suggesting that intramuscular injection of BTX-A could reduce muscle spasms. This is consistent with other relevant reports¹², and improves FMA, FIM and BBS function scores. Compared with the control group, functional scores of observation group and treatment group showed improved ($p < 0.05$). The results were better in the treatment group than in the observation and the control group, indicating that during early stroke recovery, reduced muscle spasms favor limb recovery. In the third month after treatment, CSI changes were no longer obvious between the control and observation group, with the difference being not statistically significant ($p > 0.05$). However, the differences were significant between the treatment group and the other two groups ($p < 0.05$), but the FMA, BBS and FIM scores improved significantly compared to those before treatment. The results indicated that BTX-A was effective in easing muscle spasms for about three months. However, when BTX-A reduced muscle spasms, if the patient continued to taking anticonvulsant drugs (used in preventing abnormal muscle spasms) was not conducive to early functional recovery but, interestingly, the effect of rehabilitation becomes significantly better after three months. These suggested that the BTX-A antispasmodic efficacy and its relevance in movement improvement were not proportional, which was also consistent with other reports¹². Significant differences in FMA, BBS and FIM scores were observed when comparing the treatment group with the other two groups ($p < 0.05$). In addition to BTX-A, continuous orthotic stretches could reduce muscle spasms, leading to significant improvements in BBS, FMA and FIM indicators in the treatment group. This suggests that anticonvulsant treatment is effective in improving movement. However, there is still a lack of evidence for the correlation. Further long-term clinical observation and more samples are needed.

Conclusions

Brain plasticity plays an important role in recovery after a stroke¹³. Devers suggested classic orthotics can control abnormal movements and spasticity, prevent and correct deformity, and control involuntary movements in 1966¹⁴. With improved efficiency in stroke rehabilitation, lower limb orthotics have changed: (1) They can enhance the body's sensory information input from the plantar sources and stimulate proprioception, which is conducive to upright response and reconstruction of the equilibrium reaction mechanisms, promoting early standing and walking. Studies have shown¹⁵ that on a stable support surface, the proprioceptive effect on balance accounts for about 70%, indicating that proprioception is most important for maintaining balance; (2) They place the ankle in a neutral position or slight flexion, which prevents or delays foot drop caused by a weak ankle, which helps maintain the correct posture when walking⁴; (3) They help the ankle joint remain fixed so as to correct varus, improve movement, supportive and landing stability¹⁶; (4) They improve the ankle dorsiflexion, inhibit lower limb extensor over activity, increase dorsiflexion stability, increase the forcing capacity when stepping forward¹⁷. Despite treatment, there were always significant differences in CSI, FIM, Berg and FMA between the treatment and other two groups ($p < 0.05$), suggesting that BTX-A injection with ankle foot orthotics can reduce muscle spasm and improve walking and daily activities. The two different design types of ankle foot brace used in this study can both control the ankle and foot movement on the sagittal and coronal planes, reducing spasticity, and improving balance and walking. Wearing orthotics, because the ankle is being controlled, the knee and hip are subject to different degrees of impact when in motion, thus, limiting the ankle dorsiflexion, and making it difficult for hip flexion. So, patients are more inclined to hip flexion and external rotation¹⁸. Wearing a dynamic ankle foot brace, the physiological ankle plantar flexion and dorsiflexion can be resolved when walking, making the ankle movement more natural¹⁹. Therefore, it is necessary to make better choices between fixed and dynamic equipment according to the functional status of the knee and the hip after stroke. Studies also show that dynamic ankle foot braces are better than the fixed types for walking and daily activities^{20,21}.

However, further observation is needed to explore their role in breaking the hemiplegic spastic pattern.

Due to early intervention with BTX-A to reduce muscle spasms and the injury, spasms relief is essential for the rehabilitation of hemiplegia²². Orthotic treatment plays an effective role not only in controlling abnormal movements and spasms, but also in preventing and correcting deformity.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

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