

Effect of Baimai Ointment and Botulinum Toxin Type A in the Treatment of Tip-Foot in Children with Spastic Cerebral Palsy

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Wu *et al.*: Baimai Ointment and Botulinum Toxin Type A on Spastic Cerebral Palsy

The main objective of this study is to determine the clinical efficacy of different drugs (Baimai ointment, botulinum toxin type A) in the treatment of spastic cerebral palsy in children with pointed feet. 60 subjects from Ningbo Rehabilitation Hospital (research group n=30 and control group n=30) were all given rehabilitation training. The research group was given Baimai ointment and the control group was given botulinum toxin type A. After treatment, the lower limb spasticity, triceps muscle tension, ankle joint passive dorsiflexion angle improvement, activities of daily living ability and intelligence level of the two groups were recorded and close attention was paid to the adverse drug reactions in the process of medication. Compared with the control group, lower limb spasticity, triceps muscle tension, ankle joint passive dorsiflexion angle and activity of daily living were better in the research group ($p < 0.05$). There was no significant difference in intellectual development between the two groups and there was no serious adverse drug reaction ($p > 0.05$). The application of Baimai ointment on pointed feet of patients with spastic cerebral palsy has high safety and good curative effect.

Key words: Baimai ointment, botulinum toxin type A, cerebral palsy, adverse drug reactions

An important complication in children with spastic cerebral palsy is pointed feet and regarding the mechanism of the occurrence of pointed feet, it is believed that the lower limb paralysis or muscle spasm caused by cerebral palsy occurs due to children's brain damage in the mother womb or after birth, which limits the joint movement and lead to the ankle joint being in an abnormal position for a long time^[1]. As a result of joint immobilization, tighter connective tissue is formed. In the absence of a counter pulling force, it is easy to lead to further ankle fixation, such that a pointed foot is formed. The main reason for the development of pointed toes is the increased tension of the triceps calf i.e., the gastrocnemius and soleus muscles. At present, the treatment methods of pointed feet mainly include exercise therapy, orthosis use, botulinum toxin injection, electromyography biofeedback therapy, acupuncture, massage and drug therapy, etc. This article mainly discusses about the effect of botulinum toxin injection and Baimai ointment as selected drug therapy.

Chinese Tibetan medicine believes that the pulse of

the human body can reflect the health of the human body. Among them, the Bai pulse and the black pulse are two special pulse patterns in Tibetan medicine, which respectively represent different physical conditions. Bai pulse refers to the white, cloudy or stagnant texture of the pulse. In Tibetan medicine, Bai pulse is often seen as a sign of cold dampness or phlegm in the body. On this basis, Baimai ointment was produced for external use. The main ingredients of Baimai ointment are turmeric, Yang Qi stone, Amomi Fructus Rotundus, dried ginger, sweet pine, Nardostachyos Radix et Rhizoma, synthetic musk, licorice, alkali flower, pepper, *Acorus calamus* L., fennel, etc. Baimai ointment is mainly used to treat symptoms such as claudication, paralysis, hand and foot spasm and it is an external drug. Botulinum toxin type A is produced by the *botulinum* bacterium. As a typical neuro exotoxin, its pharmacological mechanism relies on inhibiting the release of acetylcholine vesicles at the neuromuscular end, blocking neuromuscular transmission and achieving the purpose of relieving muscle spasms. Botulinum toxin type A is mainly used clinically in plastic

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surgery and also in the treatment of spastic cerebral palsy. Under the condition of strictly controlling the dosage, botulinum toxin type A has high safety and few side effects. However, as a toxin, when an adverse drug reaction occurs, its outcome is irreversible. In this study, different drug regimens were used to explore the drug value of pointy feet in children with spastic cerebral palsy.

MATERIALS AND METHODS

Sources of information:

The research data comes from 60 children with spastic cerebral palsy and pointed feet admitted to the Children's Rehabilitation Department of Ningbo Rehabilitation Hospital from December 2020 to December 2022. According to the odd-even day allocation method, 30 patients with an odd number of dates were included in the research group and 30 patients with an even number of dates were included in the control group. All the children's guardians participated in the experiment and signed the relevant consent form. This study was approved by the Ethics Committee of Ningbo Rehabilitation Hospital (Ethics approval number: 2023-013). There was no significant difference between the two groups in terms of age, gender, type and Gross Motor Function Classification System (GMFCS) grading ($p > 0.05$) (Table 1).

Inclusion criteria:

Children should meet the diagnostic and classification criteria of cerebral palsy and the classification was spastic type. Age 2-7 y old with different degrees of pointed foot, triceps muscle tension through Modified Ashworth Scale (MAS) grade \geq II; GMFCS grading value was between I-IV.

Exclusion criteria:

Children accompanied by epilepsy without complete control; use of antispasmodic drugs or botulinum toxin injection within 6 mo before treatment; corrective surgery was performed within 6 mo before treatment; severe intellectual disability, hearing impairment or other serious childhood diseases; except triceps, the muscle tension of the other muscle groups of the lower limbs was more than grade I according to MAS.

Research methods:

All patients should be supplemented with

rehabilitation training. The research group was treated with Baimai ointment and massage, and the control group was treated with botulinum toxin type A injection.

Research group: Baimai ointment was produced by Xizang Qizheng Tibetan Medicine Co., Ltd, with a specification of 20 g and approval number of Chinese Medicine Z20043178. After the rehabilitation training, the Baimai ointment was applied to the triceps of the calf every morning and afternoon, according to the application path of Baimai in Tibetan medicine and supplemented by massage for 10 min. Each application dose was 5 g and the duration was 3 mo.

Control group: Type A botulinum toxin was produced by Lanzhou Institute of Biological Products, its specification was 100 U and its main component was freeze-dried crystalline botulinum toxin type A powder. Before injection, it was diluted to 25 U/ml and aspirated with a 1 ml syringe needle. Before the injection, the child was placed in the prone or supine position and the target muscle injection point was determined by ultrasound. The nerve tissue and blood vessels of the child must be avoided during the injection. After the injection, the physical characteristics of the patient should be closely monitored. After injection, massage and bathing the injection area are prohibited and the treatment cycle was 3 mo.

Rehabilitation training: Relaxation of spastic muscle training, which is a passive movement method, using the stretch method to expand the range of motion of the ankle joint. Muscle strength training is mainly for ankle flexion and extension by using the active movement method. Standing and walking posture training is mainly training the full foot, toe and sole standing, and training the walking coordination ability. The training lasted for 30 min in the morning and afternoon every day, one course per month, a total of 3 mo and 3 courses.

Observation indicators and evaluation criteria:

The lower limb spasticity of the two groups was compared by using the Comprehensive Spasticity Scale (CSS). The CSS was developed to evaluate several types of muscle spasticity disorders including idiopathic spastic torticollis, idiopathic spastic torsion spasm and idiopathic spastic limb dyskinesia, etc. The CSS provides a method for comprehensively assessing the severity of spasticity symptoms by

combining the patient's subjective responses and objective observations. Since then, CSS has been widely used in clinical and research fields. The scale contains a total of 16 points and includes three aspects: Achilles tendon reflex, ankle plantar flexor muscle group tension and ankle clonus. Evaluation criteria were no spasticity under 7 points; 7-9 points (excluding 7 points) indicates mild spasticity; 10-12 indicates moderate spasticity; 13 to 16 points indicates severe spasticity.

The triceps muscle tension of the two groups was compared and spasticity rating scale (MAS) was used for grading. The scale was divided into 6 levels: 0, I, I⁺, II, III, IV and the higher the level, the more severe the spasticity.

Improvement in Bare Joint Passive Dorsiflexion Angle (BJPDN) was compared and measured using a joint goniometer. The normal standard is characterized as 60°-70°. The normal rate of BJPDN was compared between the two groups.

Activities of daily living were assessed and compared using the Modified Barthel Index (MBI) scale. The MBI scale was divided into five levels as complete dependence, maximum assistance, moderate assistance, minimum assistance and complete independence. The items involved bathing, eating, dressing and other aspects. The total score was 100 and the higher the score indicates the stronger the independent ability of the patient. A score ≥ 60 was defined as mild functional impairment, indicating that the patient could live independently. Scores

≥ 41 and < 60 were rated as moderate disability, indicating a need for help from others to complete daily activities. A score of less than 41 was defined as severe disability, indicating complete need for care.

The intelligence level of the two groups after medication was compared. The Child Development Center of China (CDCC) scale developed by the Institute of Psychology of Chinese Academy of Sciences was used for evaluation, which covered Mental Developmental Index (MDI) and Psychomotor Developmental Index (PDI). The developmental index above 120 points was considered as excellent, 110-119 points as upper middle, 90-109 points as medium intelligence, 80-89 points as lower middle, 70-79 points as critical state and below 69 points as mental defect. The incidence of adverse reactions in the two groups of patients was recorded and compared.

Data processing:

All data in this study were processed by using Statistical Package for Social Sciences (SPSS) 16.0 software, t-test was used to compare the two groups and $p < 0.05$ was considered statistically significant.

RESULTS AND DISCUSSION

The lower limb spasticity of the two groups was compared and there was no difference in the CSS scores between the two groups before medication ($p > 0.05$). The CSS scores in the Baimai ointment group after medication were significantly lower than those in the control group ($p < 0.05$) (Table 2).

TABLE 1: COMPARISON OF GENERAL INFORMATION OF TWO GROUPS OF CHILDREN ($\bar{x} \pm s$)

General information	Research group	Control group	p
n	30	30	
Gender	15/15	16/14	0.797
Age (months)	42.17 \pm 18.17	43.07 \pm 17.01	0.638
Classification (hemiplegia/diplegia/quadruplegia)	5/20/5	6/19/5	0.890
GMFCS classification (I/II/III/IV)	5/11/13/1	4/10/14/2	0.912

TABLE 2: COMPARISON OF CSS SCORES BETWEEN THE TWO GROUPS OF PATIENTS WITH DIFFERENT MEDICATION REGIMENS ($\bar{x} \pm s$)

Group	n	Before medication	After medication	Value of difference
Research	30	12.36 \pm 1.62	6.42 \pm 0.56	5.94 \pm 1.06
Control	30	12.56 \pm 1.58	8.16 \pm 0.72	4.4 \pm 0.86
t		0.13	2.36	1.92
p		>0.05	<0.05	<0.05

Triceps muscle tension was compared between the two groups before and after medication. Taking grade II and above as the standard of good recovery, 28 patients in the research group recovered well after treatment, accounting for 93.33 %. In the control group, 26 patients recovered well after treatment, accounting for 86.67 %. The effect of the research group was better than that of the control group ($p < 0.05$). This indicates that Baimai ointment is superior to botulinum toxin type A in improving muscle tone in the triceps muscle of the calf in patients (Table 3).

There was no significant difference in the left and right foot dorsiflexion angles between the two groups of patients before medication ($p > 0.05$). The BJPND of the research group was within the normal range after medication. Comparing the two groups, the improvement of BJPND in the research group was better than that in the control group ($p < 0.05$). This indicates that Baimai ointment is more effective than botulinum toxin type A in improving the passive dorsiflexion angle of the ankle joint in patients (Table 4).

Activities of daily living between the two groups were

compared and there was no significant difference in MBI scores between the two groups before treatment ($p > 0.05$). The MBI score of the research group was significantly higher than that of the control group ($p < 0.05$). The within-group difference was large in both groups, indicating that the two drugs were effective. The difference value of the research group was higher than that of the control group, indicating that the drug effect of the research group was better than that of the control group (Table 5).

There was no significant difference between the two groups of children's intelligence level indicators MDI and PDI after medication. Compared within the group, the CDCC indexes of the two groups were significantly different from those before treatment. The results proved that both drugs can improve intelligence in children, but there was no significant difference between the two drugs (Table 6). Adverse drug reactions between the two groups were compared and no adverse drug reactions were found in the two groups. This indicates the high safety profile of both drugs.

TABLE 3: COMPARISON OF MAS GRADING BETWEEN THE TWO GROUPS BEFORE AND AFTER MEDICATION (%)

Group	Classes	Before medication	After medication
Research	Class I	0	1 (3.33)
	Class I*	0	9 (30)
	Class II	17 (56.67)	18 (60)
	Class III	12 (40)	2 (6.67)
	Class IV	1 (3.33)	0
Control	Class I	0	0
	Class I*	0	5 (16.67)
	Class II	17 (56.67)	21 (70)
	Class III	11 (36.67)	3 (10)
	Class IV	2 (6.67)	1 (3.33)

Note: Comparison between the two groups, $p_{\text{before treatment}} > 0.05$, $p_{\text{after treatment}} < 0.05$

TABLE 4: COMPARISON OF DORSIFLEXION ANGLES OF BOTH FEET BEFORE AND AFTER MEDICATION IN THE TWO GROUPS ($\bar{x} \pm s$)

Group	n	Dorsiflexion angle of the left foot		Dorsiflexion angle of the right foot	
		Before medication	After medication	Before medication	After medication
Research	30	86.2±5.8	68.2±5.4	85.6±6.1	69.6±5.8
Control	30	86.4±5.7	72.5±5.6	85.5±6.0	73.2±5.9
t		0.11	1.86	0.11	1.84
p		>0.05	<0.05	>0.05	<0.05

TABLE 5: COMPARISON OF MBI SCORES BETWEEN THE TWO GROUPS BEFORE AND AFTER MEDICATION ($\bar{x}\pm s$)

Group	n	Before medication	After medication	Value of difference
Research	30	38.66±5.12	72.18±6.12	33.52±1.0
Control	30	38.92±5.16	64.36±6.08	25.44±0.92
t		0.21	2.23	2.62
p		>0.05	<0.05	<0.05

TABLE 6: COMPARISON OF MDI AND PDI OF CHILDREN BEFORE AND AFTER MEDICATION IN THE TWO GROUPS ($\bar{x}\pm s$)

Group	n	MDI		PDI	
		Before medication	After medication	Before medication	After medication
Research	30	86.24±6.36	96.54±7.62	86.46±7.48	96.62±7.58
Control	30	86.38±6.82	95.42±7.44	86.34±6.54	95.82±6.38
t		0.065	0.042	0.066	0.042
p		>0.05	>0.05	>0.05	>0.05

According to the theory of Tibetan medicine, the human body is composed of the white and black veins. White veins dominate the human nervous system and black veins dominate the human blood circulation system^[2]. Baimai ointment is derived from the Longevity Beads String book written by Tibetan pharmacists, which belongs to the Tibetan medicine for the diagnosis and treatment of Baimai disease. Baimai ointment is a Tibetan medicine for the treatment of Baimai disease, which adopts Tibetan medicine application therapy. This treatment follows three steps which includes apply, knead and wipe. It can bring drug efficacy directly from the pores to the capillaries. Turmeric contained in Baimai ointment has the effect of detoxifying and removing putrescence, Amomi Fructus Rotundus can stimulate the spleen and stomach, Nardostachyos Radix et Rhizoma has the effect of clearing heat and detoxifying, dispelling cold and swelling, Yang Qi stone is beneficial to muscles and veins, musk is beneficial to dredging collaterals, fennel has the effect of regulating qi and relieving pain, *Acorus calamus* L. can revive the mind and alkali flower can remove blood stasis and generate new blood^[3]. Together, these formulas have the effect of activating blood circulation, removing blood stasis, activating meridian-collaterals, dispelling wind and relieving obstruction. Specifically, in terms of the tip-foot of children with spastic cerebral palsy, Baimai ointment can repair the damaged neurons and promote local microcirculation, which has played a certain role in the recovery of the nervous system of patients^[4-6]. The tip-foot problem in the children is mainly caused by contracture of the Achilles tendon and spasm of the

triceps muscle. This situation will lead to a significant reduction in the support surface of the affected foot, which will reduce the stability of standing and further cause abnormal positions such as compensatory hyperextension of the knee joint and aggravation of the ankle-foot varus. The core of solving these problems is to deal with the triceps spasm and Achilles tendon contracture. Only by solving these two problems, we can ensure the maintenance of the normal biomechanical standing and walking problems of the human body. Baimai ointment is a traditional Chinese medicine. According to modern medicine, Baimai ointment has the effects of promoting fracture healing, improving microcirculation, improving cerebral ischemia, promoting nerve cell regeneration and nerve injury protection and has the effects of promoting the recovery of rats with Achilles tendon rupture model, promoting hematoma absorption, analgesia and anti-inflammation^[7]. As a topical medicine, Baimai ointment can avoid contact with blood vessels, intestine and stomach, and reduce the possibility of adverse reactions. Therefore, no adverse drug reactions were observed in this study. It has been proved that the direct action of Baimai ointment on the muscle site of the patient can make the drug highly effective in the local target tissue, thereby maximizing the absorption of the drug. Gong *et al.* conducted a study on 120 patients with cerebral infarction combined with hemiplegia^[8]. The treatment group was additionally treated with Baimai ointment. The results confirmed that Baimai ointment could effectively improve the muscle tension in the acute phase and improve the limb motor ability of the patients. Li *et al.* treated stroke patients with flaccid

paralysis by applying Baimai ointment and the results showed that Baimai ointment could promote hand dysfunction in stroke patients with long-lasting effects^[9]. Baimai ointment is effective for nerve repair, thus promoting the recovery of limb function.

Botulinum toxin type A is a neurotoxin produced by the bacterium *botulinum*. It exists in the form of *botulinum*. In the final analysis, botulinum toxin type A is a poison, but it is used as a medicine. Studies have shown that after entering the human body, botulinum toxin type A can release toxin proteins and prevent the transmission of neuromuscular signals, which is clinically effective^[10]. Botulinum toxin type A needs to be injected with normal saline. The target position muscle will reduce the excitation state of voluntary movement and nerve electrical stimulation^[11]. And this change does not lead to real pathological changes such as muscle fiber deformation, death and fibrosis. Triceps spasm is the main manifestation of toes in children with spastic cerebral palsy. The mechanism of muscle spasms is complex, including excessive muscle spindle movement, abnormally excited spinal nerve segments and frequent activity of motor neurons^[12]. It is generally believed that the damage to the central nervous system will lead to the obstruction or abnormality of the high central nervous system to the spinal cord stretch reflex signal, so that the stretch reflex is too enhanced or abnormally sensitive^[13]. The core processing pathway for muscle spasms is to repair muscle tone. Botulinum toxin type A is injected directly into the muscle, which blocks the nerve impulse between the nerve and the muscle and relaxes the over contracted small muscle, thus reducing muscle tension. So in this study, botulinum toxin type A also performed very well. Botulinum toxin type A is injected directly into the muscle without passing through the blood vessels and intestinal tract, which has little damage to the cardiovascular, cerebrovascular vessels and gastrointestinal tract, and showed high safety. Therefore, in this study, no adverse drug reactions were found. Some researchers have found that the effective time of botulinum toxin type A is generally 3-6 mo, and if no rehabilitation training is given during the medication period, the effect will be very limited. Some scholars pointed out that the role of botulinum toxin type A is not to improve the patient's motor function, but to relieve the patient's muscle spasm and rehabilitation training on this basis can improve the patient's motor function^[14]. The general

conclusion is that botulinum toxin type A can inhibit the transmission of nerve ending signals, thereby reducing muscle tension.

In this study, the researchers believe that the core of treating pointed feet in children with spastic cerebral palsy is to solve the problems of Achilles tendon contracture and calf triceps spasm. Comparing Baimai ointment with botulinum toxin type A, the two drugs have certain effects under the premise of rehabilitation training and will not affect the intelligence of the children, and no adverse drug events have occurred. But overall, Baimai ointment is more effective and convenient to use, and it is worth recommending.

Conflict of interests:

The authors declared no conflict of interest.

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