Effect Analysis of Botox Combined with Rehabilitation Training on Upper Limb Spasm after Hemiplegia

WEI XIAO, JING ZHAO*, LIN LI, CHUN-YING CHEN AND JIE GUO

Department of Rehabilitation Medicine, Zhejiang Hospital, Hangzhou, Zhejiang 310030, China

To analyze the effect of botox on upper limb spasm after hemiplegia after stroke under the background of rehabilitation training is the main objective of the study. The data was collected from 100 patients with upper limb spasm after hemiplegia after stroke treated in Rehabilitation Medicine Department of Zhejiang Hospital from May 2020 to June 2022. These patients were randomly divided into 50 each and included in the study group and the control group. The study group received botox therapy in the context of rehabilitation training, while the control group only received rehabilitation training. The effects of the two groups were compared after treatment. After treatment by different methods, modified Ashworth scale, Fugl-Meyer assessment, the modified Barthel index, specific quality of life scale scores and total effective rate of the study group were better than those of the control group ($p<0.05$). Botulinum toxin combined with rehabilitation training has obvious effect on upper limb spasticity of hemiplegia after stroke, which can reduce muscle tension, effectively relieve the degree of upper limb spasticity, improve the upper limb motor function and enhance the ability of living. The use of botulinum toxin in rehabilitation training is worthy of promotion.

Key words: Botulinum toxin, rehabilitation training, spasticity of the upper limbs, motor function

Upper limb spasticity often occurs after stroke and about 65 % of post-stroke patients have upper limb spasticity symptoms[1]. Functional recovery of hemiplegic patients with upper limb spasticity after stroke is one of the core tasks of rehabilitation departments in hospitals. At present, acupuncture and rehabilitation training are mostly used and botulinum toxin injection is used in a few hospitals. Botulinum toxin is a neurotoxin protein produced by *Clostridium botulinum* in the process of reproduction. Botulinum toxins are 150 kDa polypeptides that consist of a 100 kDa Heavy (H) chain and a 50 kD Light (L) chain linked by a disulfur chain. According to their toxicity and antigenicity, they can be divided into 8 types: A, B, Ca, Cb, D, E, F and G. Botulinum toxins are one of the most toxic natural substances and one of the most toxic proteins in the world. 1 mg of purified crystalline botulinum toxin can kill 200 million mice and has a half lethal dose of 40 IU/kg in humans. But the property is stable, easy to produce, purify and refine. Therefore, it was first used in experimental research and clinical practice. Botulinum toxin, produced by *Clostridium botulinum*, is a typical type A-B neurotoxin. It inhibits the release of acetylcholine vesicles at the neuromuscular junction, blocks the impulse conduction at the neuromuscular junction, causes muscle paralysis and has the effect of relieving muscle spasms. At present, botulinum toxin is mainly used in the field of cosmetic and plastic surgery, and the application of botulinum toxin in the treatment of upper limb spasticity after stroke is relatively rare. In this paper, the actual effect of botulinum toxin combined with rehabilitation training in the treatment of hemiplegic upper limb spasm after stroke was analyzed.

MATERIALS AND METHODS

General information:

A total of 100 patients with upper limb spasm after hemiplegia after stroke admitted to the Department of Rehabilitation Medicine of Zhejiang Hospital from May 2020 to June 2022 were randomly divided into study group and control group, with 50 patients in each group. There were 29 males and 21 females in the study group, with an average age of 59.28±4.18 y, average disease duration of 2.16±0.32 mo, 31 patients of cerebral hemorrhage and 17 patients of cerebral infarction. There were 28 males

***Address for correspondence**
E-mail: jjz98698@163.com

and 22 females in the control group, with an average age of 58.62±4.08 y, average disease duration of 2.14±0.31 mo, 30 patients of cerebral hemorrhage and 18 patients of cerebral infarction. There was no significant difference in the data between the two groups, which could be used as a comparative study.

Inclusion criteria: The inclusion criteria were as follows. Cerebral hemorrhage and cerebral infarction met the "Chinese Guidelines for the Diagnosis and Treatment of Acute Ischemic Stroke (2021 edition)"; the upper limb spasticity was above grade 3 according to modified Ashworth criteria and patients signed the informed consent form.

Exclusion criteria: Patients were still in the treatment period of stroke and their condition was unstable; severe cardiovascular disease, diabetes, neurological disease, hepatic and renal insufficiency; blood system diseases, immune system diseases; pregnant women, lactating women and botulinum toxin allergy.

Research methods:

The study group was treated with botulinum toxin injection for rehabilitation training and the control group was treated with rehabilitation training. The treatment time of the two groups was 4 w.

Rehabilitation training: Progressive rehabilitation training method was used in rehabilitation training. It was divided into three periods-The preparation period, the stable period and the recovery period. The preparation period was mainly in good posture training. The first is lateral position training, which measures the extension of the elbow joint back and forth, the five fingers are open and the palm is up. Ten elbow movements were considered as one set and three sets as one training session. According to the actual situation of the patient, the patient was asked to sit and stand, swing the shoulders from side to side, 10 times for one group and total 3 groups for one training and daily clenching and opening training for not less than 200 times. The pattern of reflex inhibition was dominant in the stable phase. The abnormal postures of elbow extension and wrist extension were corrected by nurses, and supplemented with training of elbow extension, wrist movement, and finger joint contraction. In the recovery period, daily life training is the main part and the goal is to allow the patient to achieve self-care. For example, let the patient wear clothes, take small objects, drink a cup of water, type and other daily life, and increase the weight appropriately according to the recovery situation. During the whole rehabilitation training, the patient's physical condition should be closely monitored to avoid fatigue or muscle pain.

Botulinum toxin injection: Botulinum Toxin Type-A (BTX-A) for injection produced by Lanzhou Institute of Biological Products, Ministry of Health was used for botulinum toxin injection. BTX-A was used as 100 Units (U) per branch. It should be diluted to 50 U/ml before injection. In order to prevent allergic reaction, 1:1000 epinephrine and oxygen should be prepared. The injection should be performed with the patient in the supine position with his arms at his sides and routine disinfection should be performed after the injection. The injection points were selected from the intramuscular area of the upper limb spasm area, 3-5 muscles were selected each time and each injection point was not more than 5. The distance of each injection point was about 3 cm. The total dose of botulinum toxin was 200 U. After the injection, the physical characteristics of the patient should be closely monitored.

Research indicators and evaluation criteria:

The Modified Ashworth Scale (MAS) rating of the two groups before and after treatment was compared: MAS rating is widely used in the evaluation of spasticity, which is divided into 6 grades: 0, I, I^{+}, II, III, IV, the higher the grade, the more severe the spasticity. After treatment, the upper limb spasticity of patients in the two groups was evaluated by MAS rating and scored according to MAS.

The Fugl-Meyer Assessment (FMA) scores of the two groups before and after treatment were compared: The patient's upper limb movement is an important indicator of upper limb spasticity. The FMA score mainly assesses the motor function of the upper limbs. It has 33 items, each with the same score and a total score of 66 points. The higher the total score, the better the upper limb motor function.

The Modified Barthel Index (MBI) scores of the two groups before and after treatment were compared: The ability to perform activities of daily living is also an important indicator of upper limb spasticity. The MBI focuses on activities of daily living, which is divided into five levels: Complete dependence, maximum assistance, moderate assistance, minimum assistance and complete independence. The item involves bathing, eating, dressing and other aspects. The total score is 100 and the higher the score, the stronger the independent

ability. 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 <41 was defined as severe disability, indicating complete need for care.

The Specific Quality of Life Scale (SS-QOL) scores before and after treatment was compared between the two groups: SS-QOL was developed by Williams and his colleagues in 1999 based on the experience of previous scales. SS-QOL was the first patient-centered scale for stroke patients. It included 12 domains and 49 items, such as energy, family role, language, activity, mood, personality, self-care ability, social role, thinking, upper limb function, vision, and work/labor. A 5-point scale (1-5 points) was used with higher scores indicating better health status.

The total effective rate of the two groups was compared: According to the MAS score, the patients were divided into marked effect, improvement and ineffective. If the muscle tension decreased by grade III or above, it was considered to be markedly effective; if the muscle tension decreased by grade I or above, it was considered to be improved. Total efficiency=Significant efficiency+improvement rate.

Statistical analysis:

In this paper, Statistical Package for the Social Sciences (SPSS) 16.0 software was used for data processing and t-test was used to test the two groups of data, $p<0.05$ was considered to be statistically significant.

RESULTS AND DISCUSSION

Comparison of MAS rating between the two groups before and after treatment was shown in Table 1. Before treatment, there were 44 patients with MAS score above grade III in the study group and 44 patients in the control group, with the same situation. After treatment, the MAS score of the study group was better than that of the control group ($p<0.05$), as shown in Table 1.

Comparison of FMA scores before and after treatment was shown in Table 2. There was no significant difference in admission of FMA scores between the two groups. However, after different treatments, the FMA score of the study group was higher than the control group ($p<0.05$).

Comparison of MBI scores before and after treatment was shown in Table 3. There was no significant difference in MBI score between the two groups on admission ($p>0.05$). After different treatments, the MBI score of the study group was higher than that of the control group ($p<0.05$).

SS-QOL scores before and after treatment was shown in Table 4. The SS-QOL scores of the two groups were basically the same at admission ($p>0.05$). After different treatments, the SS-QOL score of the study group was higher than the control group ($p<0.05$).

Comparison of total effective rate between the two groups was shown in Table 5. Both groups had certain curative effect, but the total effective rate of the study group (92 %) was better than that of the control group (78 %), where $p<0.05$.

Technically, botulinum toxin is not a drug, it's a toxin. Although botulinum toxin is not a drug, it is used clinically as a drug to treat diseases. At present, only China, the United States and the United Kingdom can produce botulinum toxin preparations, so the control of botulinum toxin is very important. In plastic surgery or medical cosmetology, botulinum toxin is routinely used. A bacterial exotoxin is produced by botulinum toxin during the process of reproduction and botulinum toxin can block nerve impulses between nerves and muscles, make excessive contraction of small muscles, relax and then achieve the effect of wrinkle removal.

TABLE 1: COMPARISON OF MAS SCORES BETWEEN THE TWO GROUPS BEFORE AND AFTER TREATMENT (%)

Group	n	Class c		Class I+		Class II		Class III		Class IV	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Research group	50	0	20 (40)	0	17 (34)	24 (48)	11 (22)	20 (40)	1 (2)	6 (12)	1 (2)
Control group	50	0	1 (2)	0	9 (18)	25 (50)	32 (64)	19 (38)	4 (8)	6 (12)	4 (8)

Note: Comparison between the two groups, $p_{Before\ treatment}>0.05$ and $p_{After\ treatment}<0.05$

TABLE 2: COMPARISON OF FMA SCORES BETWEEN THE TWO GROUPS BEFORE AND AFTER TREATMENT (x̄±s)

Group	n	Before treatment	After treatment
Research group	50	18.32±2.16	32.19±3.14
Control group	50	18.24±2.08	24.46±2.76
t		0.087	4.28
p		>0.05	<0.05

TABLE 3: COMPARISON OF MBI SCORES BETWEEN THE TWO GROUPS BEFORE AND AFTER TREATMENT (x̄±s)

Group	n	Before treatment	After treatment
Research group	50	39.85±4.12	68.52±7.26
Control group	50	40.02±4.08	55.48±5.96
t		0.098	3.69
p		>0.05	<0.05

TABLE 4: SS-QOL SCORES OF THE TWO GROUPS BEFORE AND AFTER TREATMENT (x̄±s)

Group	n	Before treatment	After treatment
Research group	50	124.52±11.82	169.64±18.52
Control group	50	125.35±11.86	142.56±14.28
t		0.062	2.42
p		>0.05	<0.05

TABLE 5: COMPARISON OF THE TOTAL EFFECTIVE RATE OF TREATMENT BETWEEN THE TWO GROUPS (%)

Group	n	Conspicuous effect	Get better	Void of effect	Total effectiveness
Research group	50	17	29	4 (8)	46 (92)
Control group	50	1	38	11 (22)	39 (78)
t					1.95
p					<0.05

Or it can use its characteristics of temporary paralysis of muscles, so that muscles atrophy due to loss of function, to achieve the purpose of sculpting lines. Botulinum toxins are highly toxic drugs and a certain dose can easily cause death. However, from a clinical point of view, botulinum toxin is controlled under a safe dose and its adverse events rarely occur[2]. When applied to patients with upper limb spasticity after stroke, botulinum toxin has the effect of inhibiting nerve endings and secreting acetylcholine. Its drug lasts for a long time and its paralytic effect can effectively form new nerve terminals and reduce muscle tension[3].

The symptoms of upper limb spasticity after stroke are caused by the decline or disappearance of descending inhibition caused by the damage of upper motor neurons, resulting in different degrees of involuntary contraction of muscles, showing resistance to movement[4]. It affected the recovery of upper limb function and showed elbow flexor spasm in the upper limb, especially biceps brachii spasm. Botulinum toxin can cause muscle chemical denervation and block the release of acetylcholine vesicles for several months, until the endplate repair pathway has occurred. As neuromuscular axons sproule through the re-innervation of the nerve, so that muscle recovery occurs after the formation of a new endplate. BTX-A is injected directly through muscle because it is not injected through blood vessels. So it will not flow through the blood-brain channel, forming a certain barrier. In this way, its toxicity can minimize damage to the cardiovascular and cerebrovascular vessels, and on the other hand, it can directly act on the neuromuscular axons with high affinity and produce drug effect on the receptor. Only a small amount of BTX-A remains and is cleared by the body's system through the blood circulation[5]. Therefore, in practice, botulinum toxin is controlled under the safe dose and there are few cases of central nervous system toxic side effects.

Rehabilitation training can relax the muscles of patients to a certain extent and reduce the muscle tension of patients. Rehabilitation training creates good basic conditions for injection of botulinum

toxin. In other words, the two are complementary and the injection of botulinum toxin alleviates the spasticity of the patient's upper limbs and lays the foundation for the patient's rehabilitation training. Some scholars have found that botulinum toxin has analgesic effect and can reduce the pain of patients. However, the pharmacological effect of this study has not been widely accepted. Chinese scholars, such as Xiong Guofang and Li Jinxian, believed that upper limb spasm clinically manifests the symptoms of abnormal muscle contraction. The more reason is that the obstructed movement channel will lead to abnormal activity of the limb muscles, which will compress the blood vessels near the muscle, which will consume more oxygen, so it will show abnormal contraction of the muscle in the ischemic environment[6]. The ultimate consequence of this situation is the activation of further nociceptors in the muscle through the release of bradykinin. However, these inflammatory factors can further aggravate the occurrence of muscle spasms[7]. Intramuscular injection of botulinum toxin blocks the neuromuscular transmission pathway and blocks this undesirable cycle. In essence, botulinum toxin is a foreign protein with immunogenicity[8]. Studies have confirmed that some patients have no response to botulinum toxin injection and some patients begin to have no response after several injections, which may be due to primary non-response and secondary non-response, and the root cause may be antibody reasons[9]. However, the relationship between antibodies and efficacy has not been further confirmed. It has been suggested that botulinum toxin injection can cause pain and fatigue at the injection site[10]. There are also data suggesting that after small doses of botulinum toxin injection, single fiber Electromyography (EMG) abnormalities occur in muscles far from the site of injection[11].

This study shows that simple rehabilitation training is helpful for patients with upper limb spasticity, which can effectively improve their motor function and living activity ability. However, after the injection of botulinum toxin, the patient's motor function and living activity ability were greatly improved. In conclusion, the application of botulinum toxin combined with rehabilitation training in patients with upper limb spasticity after stroke can improve the upper limb motor function of patients, improve the ability of daily living, improve the quality of life of patients, and improve the total effective rate of treatment. On the premise of strict control of dose and safety, it should be widely promoted.

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Conflict of interests:

The authors declared no conflict of interest.

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