Showa Univ J Med Sci **29**(2), 193～200, June 2017

Original

Comparison of Plantar Pressure and Plantar Contact Area before and after Botulinum Toxin Type A (BoNT-A) Therapy in Stroke Patients with Lower Limb Spasticity

Nobuyuki KAWATE*[1, 2], Miyuki MATSUMOTO[1] and Shinsuke IIJIMA[1, 2]

Abstract: The effectiveness of botulinum toxin type A (BoNT-A) therapy for reducing muscle spasticity has been reported. We examined changes in the plantar contact area and plantar pressure after BoNT-A injection therapy in stroke patients with spastic hemiparesis. The study participants were 12 male hemiparetic stroke patients treated in our outpatient clinic (right hemiparesis, 7; left, 5), who were able to walk without orthoses. They were requested to walk barefoot at their normal walking speed on a sheet with pressure measurement sensors, before, and at one and three months after BoNT-A therapy. Simultaneously the maximum plantar pressures and maximum plantar contact areas of both feet during the standing phase of walking were analyzed using a pressure distribution measuring system. The ratios of the measured values for the affected side to that of the unaffected side were calculated. The mean ratio of the maximum plantar pressure of the affected / unaffected limb on standing changed from 61.5% ± 12.4% to 75.0% ± 9.5% at one month, and 61.2% ± 7.3% at three months after BoNT-A therapy. The mean maximum plantar contact area ratios also changed from 75.3% ± 11.7% to 87.9% ± 8.7% at one month and 77.8% ± 8.8% at three months. For both parameters, the ratios were significantly increased at one month after BoNT-A, compared to the other time points ($P < 0.01$). These results suggest that BoNT-A therapy reduces muscle spasticity of the lower limbs, which improves the range of motion of the ankle joints, leading to improved plantar contact during the standing phase of walking. This pressure measurement system may be useful for assessing the effectiveness of BoNT-A therapy.

Key words: stroke, muscle spasticity, botulinum toxin, gait analysis, plantar pressure

Introduction

Muscle spasticity is a common sign of upper motor neuron syndrome. It is defined as a motor disorder characterized by a velocity-dependent increase in the tonic stretch reflex with an exaggerated tendon reflex[1, 2]. It is a condition of increased muscle tone observed in patients who have sustained central nervous system damage, such as that caused by strokes. If muscle

[1] *Department of Rehabilitation Medicine, Showa University School of Medicine,* 2-1-1 Fujigaoka, Aoba-ku, Yokohama 227-8515, Japan.
[2] *Department of Rehabilitation Medicine, Fujigaoka Rehabilitation Hospital.*
* To whom corresponding should be addressed.

spasticity persists for a prolonged period, the range of motion of the joints becomes restricted due to changes in the viscoelasticity of the muscles, thereby negatively impacting the patients' activities of daily living, such as eating and dressing, and leading to the deterioration of walking ability due to equinus foot or skew foot[3]. In recent years, botulinum toxin type A (BoNT-A) therapy has received attention as a potential treatment for muscle spasticity. It is predicted that amelioration of muscle spasticity will lead to an improvement in the walking ability of hemiparetic stroke patients.

To our knowledge, no studies have examined the changes in walking ability before and after BoNT-A injection, using an objective measurement instrument. In this study, we analyzed changes in the maximum plantar pressure and maximum plantar contact area during the standing phase of walking, before and after BoNT-A injection therapy in stroke patients with spastic hemiparesis, using a pressure measurement system consisting of a sheet sensor and a pressure distribution measuring system.

Materials and methods

Study participants (*Table 1*)

Twelve male patients (mean age, 62.9 ± 7.2 years ; range, 52–77 years) who had chronic hemiparesis with a post-onset duration of over one year participated in the study. Seven patients had right hemiparesis and five had left hemiparesis, with a lower extremity Brunnstrom stage of 3–4 and modified Ashworth scale of 3–4. They were able to walk barefoot. The participants did not change their physical therapy program and there were no recurrences of

Table 1. Characteristics of patients with spasticity and BoNT-A dose

Pt.	Age	Gender	Diagnosis	Affected side	MAS	Brunnstrom stage (lower)	BoNT-A (IU)
1	56	M	CH	Left	4	III	300
2	57	M	CH	Right	4	III	300
3	77	M	CH	Right	3	III	200
4	52	M	CH	Left	4	IV	300
5	69	M	CH	Left	4	IV	300
6	62	M	CH	Right	4	IV	300
7	65	M	CH	Right	3	IV	300
8	67	M	CH	Right	3	IV	200
9	54	M	CI	Left	4	III	300
10	68	M	CI	Left	3	IV	300
11	63	M	CI	Right	3	IV	200
12	65	M	CI	Right	3	IV	300
All	62.9*	12M	8CH / 4CI	7R / 5L	6-MAS 4 6-MAS 3	4 III / 8 IV	3-200 IU 9-300 IU

BoNT-A, botulinum toxin type A ; Pt., patient number ; MAS, modified Ashworth scale ; *, mean ; M, male ; R, right ; L, left ; CI, cerebral infraction ; CH, cerebral hemorrhage.

cerebral vascular accidents during the whole study period. In addition, rehabilitation during the period was not changed.

Informed consent was obtained from each patient after a full explanation of the study was provided in writing, including the risks and benefits of BoNT-A injection therapy. This study was approved by the Ethics Committee of Showa University School of Nursing and Rehabilitation Science (approval number : 241).

BoNT-A injection

In total, 200–300 IU of BoNT-A was injected into the spastic muscles (gastrocnemius, soleus, and posterior tibial muscles) of the affected leg of each patient.

Measurement device and measurement method (Fig. 1)

The participants were requested to walk barefoot at their normal walking speed on a sheet with pressure sensors (WalkWay MW-1000, ANIMA Corp., Tokyo, Japan) before BoNT-A injection and then again at one and three months after injection. The maximum plantar pressure and maximum plantar contact area of the right and left feet during the standing phase of walking were evaluated using a pressure distribution measuring system (Predas MD-1000, ANIMA Corp., Tokyo, Japan). The ratio, expressed as a percentage, of the maximum plantar pressure on the affected side to that on the unaffected side was compared between before

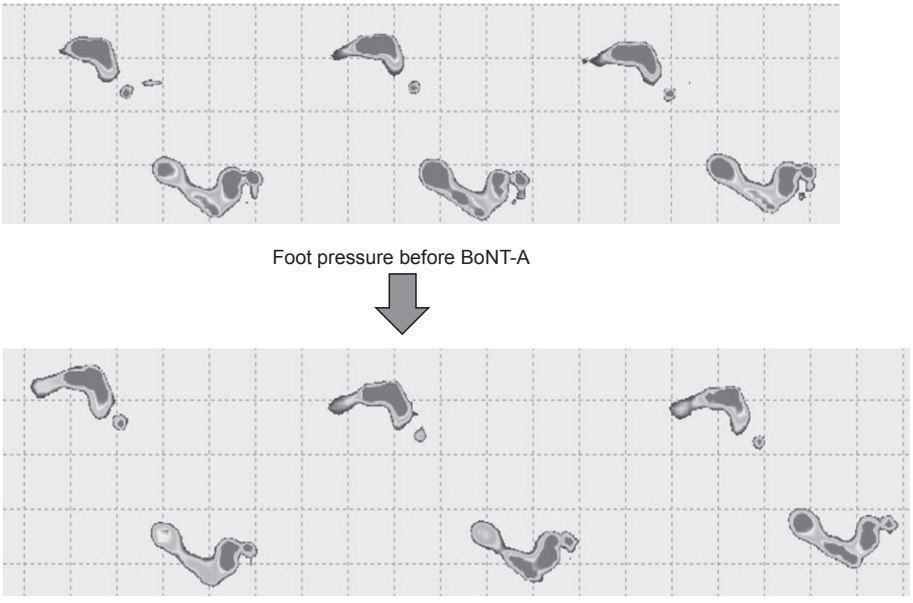

Fig. 1. Original data of foot pressure during gait
Patient 4 : 52-year-old male with left foot spasticity, Brunnstrom stage (lower) Ⅲ, injected with 300 IU botulinum toxin type A (BoNT-A). Modified Ashworth scale for dorsiflexion decreased from 4 (before BoNT-A) to 2 (one month after BoNT-A). A maximum foot pressure value was taken from both the right and left foot to calculate the ratio of affected / unaffected foot pressure.

injection, and at one and three months after injection. The ratios of the maximum plantar contact area of the affected side / unaffected side were similarly compared.

Statistical analysis

The maximum plantar pressure and plantar contact area before injection, and at one and three months after injection, were analyzed by paired one-way analysis of variance and then compared between the groups by a post-hoc test (Scheffe method) using SPSS 19.0 J (SPSS, Chicago, IL). Data were expressed as mean ± standard deviation, and the significance level was set at 5%.

Results

The modified Ashworth scale was decreased in all patients at one month after BoNT-A injection (Fig. 2). The ratio of the maximum plantar pressure of the affected / unaffected side was 61.5% ± 12.4% before BoNT-A injection, 75.0% ± 9.5% at one month after injection, and 61.2% ± 7.3% at three months after injection. The ratio was significantly increased one month after injection, compared to before injection (i.e., the difference in plantar pressure between the affected and unaffected sides was decreased), but it had returned to the pre-treatment level at three months after injection (Fig. 3). The ratio of the maximum plantar contact area of the affected / unaffected side was 75.3% ± 11.7% before BoNT-A injection, 87.9% ± 8.7% at one month after injection, and 77.8% ± 8.8% at three months after injection. The ratio was significantly increased one month after injection, compared to before injection (i.e., the difference in the plantar contact area between the affected and unaffected sides was decreased), but it had returned to the pre-treatment level at three months after injection, similar to the plantar pressure results (Fig. 4).

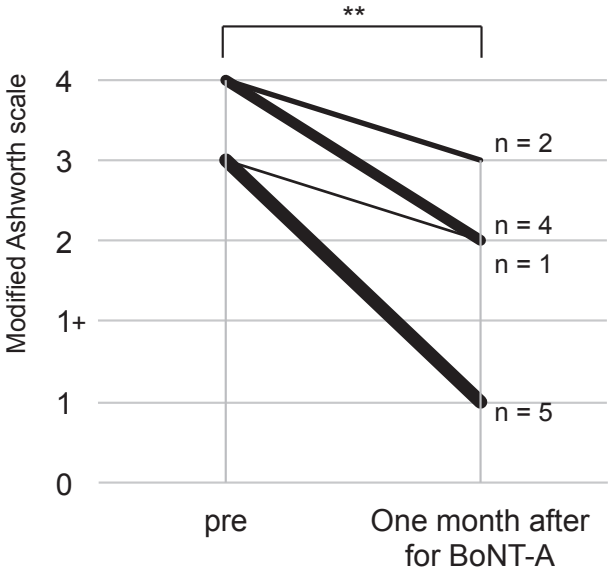

Fig. 2. Changes in modified Ashworth scale before (pre) and one month after injection of botulinum toxin type A (BoNT-A) into the spastic muscles of the lower limb. **, $P < 0.01$, pre vs. one month. n, number of patients.

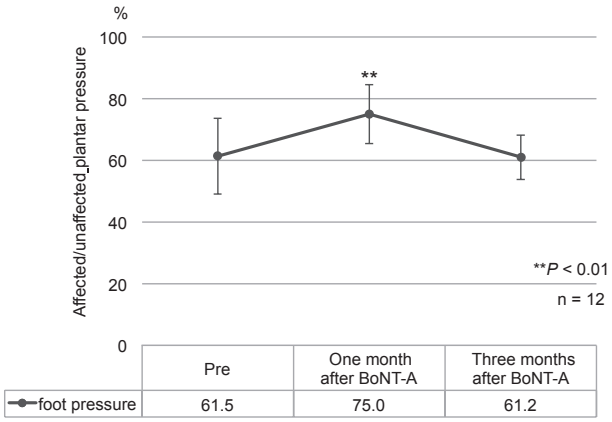

Fig. 3. Ratio of maximum plantar pressure of the affected / unaffected side before injection of BoNT-A (Pre), and one month and three months after BoNT-A.**, $P < 0.01$, compared to the other time points. BoNT-A, botulinum toxin type A.

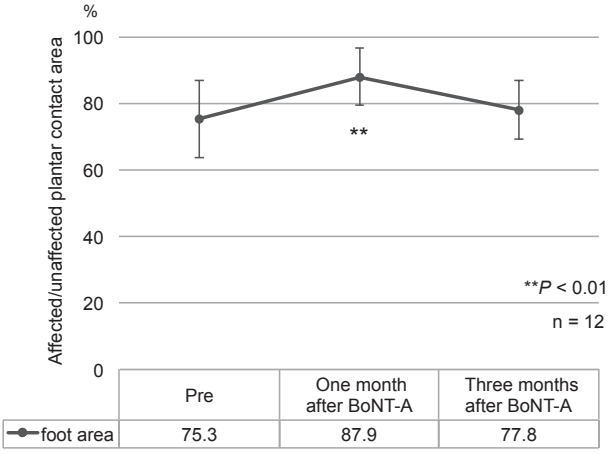

Fig. 4. Ratio of maximum plantar contact area of the affected / unaffected side before injection of BoNT-A (Pre), and one month and three months after BoNT-A.**, $P < 0.01$, compared to the other time points. BoNT-A, botulinum toxin type A.

Discussion

Muscle spasticity is observed in almost all stroke patients. If it persists for a prolonged period, patients develop range of motion restrictions in their joints due to changes in the viscoelasticity of affected muscles, which negatively impacts on their activities of daily living, and causes deterioration in their walking ability[3]. Traditional treatments for spasticity include oral antispasmogenics[4], nerve blocks targeting the motor nerve and muscular junction (motor point)[5, 6], prolonged stretching[7], orthotic treatments such as an inhibitor bar[8] or a toe spreader[9], the Vulpius method, and orthopedic procedures such as anterior tibial tendon transfer[10].

Although there is a wide variety of treatment methods, their effects are limited. The first clinical use of BoNT-A was for the treatment of strabismus, as reported by Scott in 1980[11]. Since then, BoNT-A therapy has received attention as a potential treatment for muscle spasticity. BoNT-A is a component of botulinum toxin produced by the *Clostridium botulinum* organism, which is a gram-positive anaerobic bacterium. There are seven different categories of botulinum toxin, designated types A through G. BoNT is the most toxic form, and the lethal dose of BoNT-A when inhaled by a human (70 kg) is estimated to be approximately 0.7–0.9 μg[12]. BoNT-A causes muscle relaxation by blocking the release of acetylcholine from the nerve terminal at the neuromuscular junction. This effect has led to the development of the toxin as a muscular relaxant for patients with abnormal muscle tone, such as those with spasticity and torticollis. BoNT-A is currently used for a wide variety of conditions, including spasticity, blepharospasm, unilateral facial spasm, strabismus, spasmodic strabismus, glabellar line between the eyebrows, hyperhidrosis, and hyperactive bladder. In Japan, BoNT-A was approved for the treatment of spasticity involving the upper and lower extremities in adults in 2010, and several studies have demonstrated the effectiveness of BoNT-A on muscle spasticity[13, 14].

Muscle spasticity may be related to changes in peripheral tissues and the breakdown of the central nervous system in acute stroke patients[15, 16], and a model of spasticity development for the stages of motor output reorganization after stroke has been proposed (spasticity is considered to be a manifestation of maladaptive plastic responses)[17]. Studies have shown the effects of BoNT-A on activities related to muscle stretch reflexes, such as an effect on γ-motor neurons at the neuromuscular junction, a change in stimulation of Ia muscle spindles due to degeneration of γ-neurons, decreased co-contraction, and decreased Renshaw inhibition of the H reflex[18]. In addition, a study of stroke patients has demonstrated that short-interval intracortical inhibition in the unaffected cerebral hemisphere recovers to a normal level after BoNT-A injection, suggesting an effect on the central nervous system[19]. Therefore more observations of the injured brain area and size are required in future studies.

Numerous studies have analyzed the center of foot pressure in healthy individuals while walking, by measuring the plantar pressure or contact area using pressure measurement systems, similar to the device employed in our present study. The plantar pressures and plantar contact areas are reportedly almost the same in the right and left feet of healthy individuals[20, 21]. In contrast, hemiparetic stroke patients have difficulty placing their weight on the affected leg, because their plantar contact area is reduced due to a decrease in the range of motion of the ankle joint and equinovarus foot deformity resulting from muscle spasticity. In the present study, the maximum plantar pressure and maximum plantar contact area on the affected side were 60%～70% of the unaffected side before BoNT-A injection. One month after BoNT-A injection, the maximum plantar pressure and plantar contact area on the affected side reached 70 %～90 % of the unaffected side, i.e., they were comparable to the unaffected side. These results suggest that botulinum therapy reduced the muscle spasticity of the lower limbs, which improved the range of motion of the affected ankle joints, leading to improved plantar contact during loading.

However, at three months after injection, the maximum plantar pressure and maximum plantar contact area had returned to 60%～70% of the unaffected side. It is assumed that the nerve terminals that stopped releasing acetylcholine after BoNT-A therapy regained neurotransmitter function by sprouting new nerve terminals over the period of three to four months after treatment[22]. Spasticity was therefore considered to have returned to the pre-injection level. In addition, these results suggest that the pressure measurement device used in the present study might be useful for assessing the effectiveness of BoNT-A therapy by comparing walking status before and after BoNT-A injection.

Conflict of interest disclosure

The authors have no conflicts of interest to declare.

References

1) Lance JW. Symposium synopsis. In *Feldman RG, Young RR, Koella WP, eds. Spasticity, disordered motor control.* Chicago: Year Book Medical Publisher; 1980. pp485-494.
2) Tanaka R. Mechanism of spasicity. *Jpn J Rehabil Med.* 1995;**32**:97-105. (in Japanese).
3) Kagamihara Y. Mechanism and assessment of spasticity. *J Clin Rehabil*. 2012;**21**:936-943. (in Japanese).
4) Nakanishi R, Yamanaga H, Yamade T. Pharmacotherapy of spasticity. *J Clin Rehabil*. 1993;**2**:530-535. (in Japanese).
5) Zafonte RD, Munin MC. Phenol and alcohol blocks for the treatment of spasticity. *Phys Med Rehabil Clin N Am.* 2001;**12**:817-832, vii.
6) Mezaki T, Kaji R, Hirota N, *et al*. Treatment of spasticity with muscle afferent block. *Neurology*. 1999;**53**:1156-1157.
7) Tanaka N, Shoji J, Yatsunami M, *et al.* Examination of the effect of prolonged stretch for spastic muscle. *J phys med*. 2001;**12**:193-198. (in Japanese).
8) Bronkhorst AJ, Lamb GA. An orthosis to aid in reduction of lower-limb spasticity. *Orthot Prosthet.* 1987;**41**:23-28.
9) de Saca LR , Catlin PA, Segal RL. Immediate effects of the toe spreader on the tonic toe flexion reflex. *Phys Ther.* 1994;**74**:561-571.
10) Watanabe H, Mizuma M, Kawate N, *et al.* Examination of brain strike hemiplegic patients and surgical treatments for equinovarus and hammer-toe deformity. *J Showa Med Assoc.* 2005;**65**:443-448. (in Japanese).
11) Arnon SS, Schechter R, Inglesby TV, *et al.* Botulinum toxin as a biological weapon: Medical and public health management. *JAMA*. 2001;**285**:1059-1070.
12) Kimura A, Abo M, Kawate N, *et al.* Efficacy and safety of botulinum toxin type A in treating upper limb spasticity in post-stroke patients: A multicenter, double-blind, placebo-controlled trial followed by an open-label trial. *Jpn J Rehabil Med*. 2010;**47**:714-727. (in Japanese).
13) Kimura A, Abo M, Masakado Y, *et al.* An investigation into the clinical use of botulinum toxin type A to treat post-stroke hemiplegic patients with upper and / or lower limb spasticity. *Jpn J Rehabil Med.* 2015;**52**:421-430. (in Japanese).
14) Gracies JM. Pathophysiology of spastic paresis. I: Paresis and soft tissue changes. *Muscle Nerve*. 2005;**31**:535-551.
15) Gracies JM. Pathophysiology of spastic paresis. II: Emergence of muscle overactivity. *Muscle Nerve.* 2005;**31**:552-571.
16) Swayne OB, Rothwell JC, Ward NS, *et al.* Stages of motor output reorganization after hemispheric stroke suggested by longitudinal studies of cortical physiology. *Cereb Cortex*. 2008;**18**:1909-1922.
17) Rosales RL, Arimura K, Takenaga S, *et al.* Extrafusal and intrafusal muscle effects in experimental botulinum toxin-A injection. *Muscle Nerve*. 1996;**19**:488-496.

18) Huynh W, Krishnan AV, Lin CS, *et al.* Botulinum toxin modulates cortical maladaptation in post-stroke spasticity. *Muscle Nerve*. 2013;**48**:93–99.
19) Sakurai S, Sakamoto M, Nakazawa R, *et al*. Analysis of gait of healthy women: study for classification of tracking of the center of pressure. *Rigakuryoho Kagaku.* 2007;**22**:209–213. (in Japanese).
20) Horimoto Y, Maruyama H. Characteristics of center of foot pressure path of healthy adults. *Rigakuryoho Kagaku*. 2010;**25**:687–691. (in Japanese).
21) de Pavia A, Meunier FA, Molgo J, *et al*. Functional repair of motor endplates after botulinum neurotoxin type A poisoning: biphasic switch of synaptic activity between nerve sprouts and their parent terminals. *Proc Natl Acad Sci U S A*. 1999;**96**:3200–3205.

[The publication of this paper was given a priority date]