

*Original Article***Improvement in Disability Assessment Scale after Botulinum toxin A treatment for upper limb spasticity**

Kenta Fujimura, OTR, BS,¹ Hitoshi Kagaya, MD, DMSc,² Hisae Onaka, OTR,³
 Yuki Okochi, OTR,³ Masayuki Yamada, OTR, MS,¹ Toshio Teranishi, RPT, PhD,¹
 Yoshikiyo Kanada, RPT, DMSc,¹ Eiichi Saitoh, MD, DMSc²

¹Faculty of Rehabilitation, School of Health Sciences, Fujita Health University, Toyoake, Aichi, Japan

²Department of Rehabilitation Medicine I, School of Medicine, Fujita Health University, Toyoake, Aichi, Japan

³Department of Rehabilitation, Fujita Health University Hospital, Toyoake, Aichi, Japan

ABSTRACT

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Objective: We investigated the effect of botulinum toxin type A for upper limb spasticity on activities of daily living using the Disability Assessment Scale (DAS).

Methods: The subjects were 47 patients who received botulinum therapy for upper limb spasticity. They were assessed before administration and 2, 6, and 12 weeks after administration by using the DAS, the Modified Ashworth Scale (MAS), and upper-limb-related parameters from the Fugl-Meyer Assessment (FMA).

Results: DAS scores for hygiene, dressing, and limb position improved significantly 2 and 6 weeks after administration ($p < 0.05$), but there was no significant change in pain. MAS scores exhibited significant improvement 2, 6, and 12 weeks after administration, and the total scores for FMA upper-limb parameters exhibited significant improvement 2 and 6 weeks after administration ($p < 0.05$).

Conclusion: Botulinum therapy contributes to improving not only the spasticity itself, but also to improving difficulties in activities of daily living associated with upper limb spasticity.

Key words: spasticity, BoNT-A, activities of daily

living, upper limb function, Disability Assessment Scale

Introduction

Spasticity is one of the positive symptoms of cerebrovascular disease and other upper motor neuron diseases. Approximately 20% of all first-time stroke patients exhibit spasticity 1–2 weeks, 3 months, and 18 months after the stroke, and spasticity is reported to become more severe over time [1]. Spasticity not only diminishes voluntary control of the upper and lower limbs on the affected side and their function level, but also impedes the performance of rehabilitation with the aim of improving motor paralysis. Upper limb spasticity tends to occur predominantly in the flexor muscles, in many cases causing the limb to adopt an abnormally flexed position. This impairs the patient's ability to perform many activities of daily living (ADL), including maintaining hand hygiene by hand washing and wiping, changing clothes, standing up, and walking. In terms of appearance, posture and limb position are also poor. Spasticity thus gives a strong impact.

Botulinum toxin type A (BoNT-A) is widely used in the treatment of spasticity. In addition to the Barthel Index (BI) and the Functional Independence Measure (FIM) for evaluating overall ADL, the 8-Item Disability Scale [2] and the Disability Assessment Scale (DAS) [3] can be used to evaluate the effect of upper limb spasticity on ADL performance. The BI and FIM are scales for evaluating the level of independence in ADL, but since it is unclear whether the affected or unaffected side is used in performing actions, they cannot be described as simply measuring impaired ability due to spasticity. The 8-Item Disability Scale is an evaluation tool developed to measure the effect of upper limb spasticity using a four-point scale to assess eight parameters – cleaning the palm, cutting

Correspondence: Kenta Fujimura, OTR, BS
 Faculty of Rehabilitation, School of Health Sciences, Fujita Health University, 1–98 Dengakugakubo, Kutsukake-cho, Toyoake, Aichi 470–1192, Japan.

E-mail: fujimura@fujita-hu.ac.jp

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the fingernails, putting the paretic arm through a sleeve, cleaning under the armpit, cleaning around the elbow, standing balance, walking balance, and the ability to perform an upper limb physiotherapy exercise program at home. Although this assessment does reflect upper limb spasticity, it does not take into account issues such as abnormal limb position, and the results may also be affected by other factors related to physical ability besides upper limb spasticity. The DAS is another evaluation tool developed to measure disability associated with upper limb spasticity in patients with this condition. The evaluation parameters include some that reflect hand washing and changing clothes as part of ADL, and others related to abnormal limb position and pain associated with spasticity. Patients are evaluated in an interview format, enabling the severity of the disability to be assessed (Table 1). Most studies involving DAS evaluations before and after BoNT-A administration [4–17] have focused on one treatment target from among the four DAS parameters. Simpson et al. [7] reported that DAS scores improved significantly 6 weeks after BoNT-A administration in 19 patients who chose limb position as the target out of a total of 60 cases. Kaji et al. [9] also found that DAS scores improved significantly after BoNT-A administration in 51 patients who chose limb position and 31 who chose dressing actions as the targets out of a total of 109 cases. Other studies, however, only recorded the fact that target parameters improved, without indicating the specific parameters. Spasticity may cause more than one disability, and it is unclear whether or not it is appropriate to select only a single target parameter to assess the severity of the disability. A study by Marciniak et al. [18] evaluated all four DAS parameters in 10 patients treated with BoNT-A and 11 who were given a placebo. They found a significantly greater improvement in hygiene four weeks after treatment among those in the BoNT-A group compared with the placebo group, as well as a similar trend of improved ability to execute dressing. The objective of the present study was to evaluate the disabilities associated with upper limb spasticity using all four DAS parameters,

and to identify their characteristics and changes over time.

Methods

The study subjects were 47 patients who underwent BoNT-A treatment between January 2012 and June 2014 for upper limb spasticity resulting from cerebrovascular damage. The subjects comprised 27 men and 20 women, with mean age of 56 years (19–76 years). The spasticity was caused by cerebral infarction in 17 cases, cerebral hemorrhage in 29, and subarachnoid hemorrhage in 1. The mean time from onset until BoNT-A administration was 1,552 days (median 1,337 days, range 117–5,610 days).

Difficulties in ADL were assessed by using the DAS. Spasticity was assessed according to the Modified Ashworth Scale (MAS) [19], with evaluation of the shoulder adductor, elbow flexor, forearm pronator, wrist flexor, finger proximal interphalangeal (PIP) joint flexor, and thumb interphalangeal (IP) joint flexor muscles. Motor function was assessed in terms of the total Fugl-Meyer Assessment upper extremity (FMA-U/E) score [20] and its subscales (A: shoulder/elbow/forearm; B: wrist; C: fingers; D: coordination/speed). Assessments were performed four times, specifically, before treatment and 2, 6, and 12 weeks after treatment. Written consent was obtained from the patients at each assessment.

Statistical Analysis

DAS, MAS, and FMA-U/E scores at 2, 6, and 12 weeks after BoNT-A administration were compared with those before administration. A comparison between the pretreatment DAS parameters was also performed. The Wilcoxon signed rank test, corrected by the Bonferroni method, was used for comparisons. The statistical software used was SPSS Statistics Version 21 (IBM), with $p < 0.05$ regarded as significant.

Table 1. Disability Assessment Scale (DAS) [3].

Interview with each patient to determine the extent of functional impairment according to the following scale:	
0: No disability.	
1: Mild disability (noticeable but does not significantly interfere with normal activities).	
2: Moderate disability (normal activities require increased effort and/or assistance).	
3: Severe disability (normal activities limited).	
Hygiene	The extent of maceration, ulceration, and/or palmar infection; palm and hand cleanliness; ease of cleaning; ease of nail trimming; and the degree of interference caused by hygiene-related disability in the patient's daily life.
Dressing	The difficulty or ease with which the patient could put on clothing (e.g., shirt, jacket, gloves) and the degree of interference caused by dressing-related disability in the patient's daily life.
Limb position	The amount of abnormal position of the upper limb.
Pain	The intensity of pain or discomfort related to upper limb spasticity.

Results

The muscles treated with BoNT-A were the pectoralis major in 24 patients, the biceps brachii in 31, the brachialis in 5, the brachioradialis in 1, the triceps brachii in 1, the pronator teres in 6, the flexor carpi radialis in 38, the flexor carpi ulnaris in 37, the palmaris longus in 1, the flexor digitorum profundus in 4, the flexor digitorum superficialis in 45, and the flexor pollicis longus in 23. A dose of 15–100 units was administered to each muscle.

Before BoNT-A administration, the number of patients with a DAS score of 0 (no disability) was 20 (42.6%) for hygiene, 15 (31.9%) for dressing, 15 (31.9%) for limb position, and 32 (68.1%) for pain. The corresponding numbers for those with a DAS score of 3 (severe disability) were 11 (23.4%) for hygiene, 5 (10.6%) for dressing, 11 (23.4%) for limb position, and 0 (0.0%) for pain. A comparison between the different parameters before BoNT-A administration showed that compared with pain, the level of disability was significantly higher for hygiene ($p = 0.001$), dressing ($p < 0.001$), and limb position ($p < 0.001$). Figure 1 shows the changes in DAS parameters over time after BoNT-A administration. Improvements in hygiene ($p = 0.006$, $p = 0.030$), dressing ($p = 0.001$, $p = 0.003$), and limb position ($p < 0.001$, $p = 0.003$) were evident at 2 and 6 weeks after administration. However, at 12 weeks after administration, there was no significant difference compared with the scores before administration. There was no significant change in pain

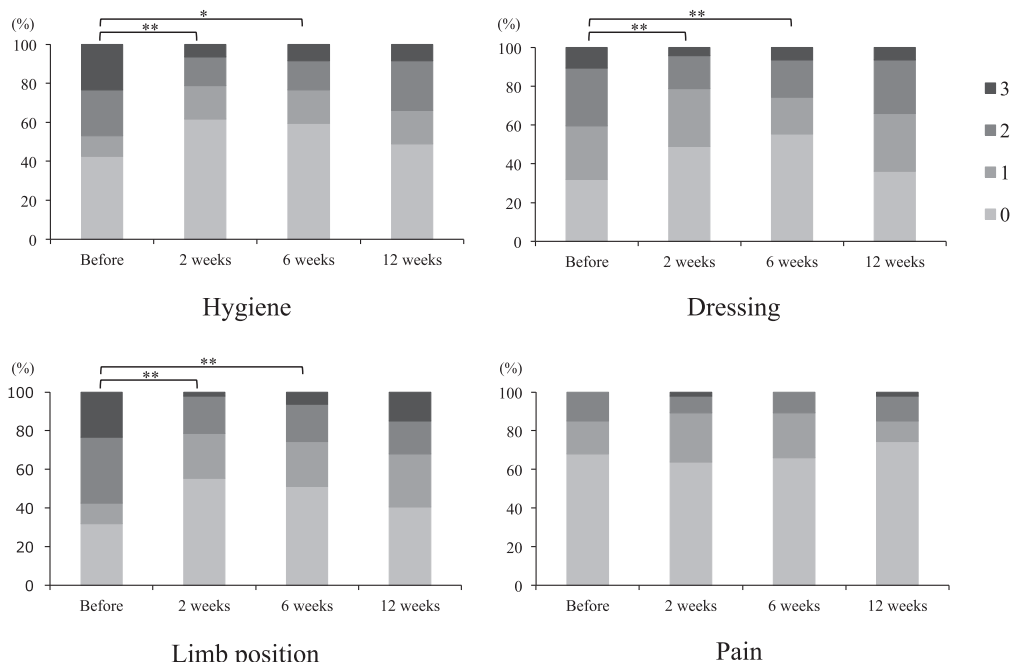
at any point after administration compared with before administration.

MAS scores for the shoulder adductor and elbow flexor muscles improved significantly at 2 weeks ($p < 0.001$) and 6 weeks ($p = 0.001$) after BoNT-A administration. Significant improvement in the scores for the forearm pronator, wrist flexor, finger PIP joint flexor, and thumb IP joint flexor muscles was evident at 2, 6, and 12 weeks after administration (Table 2).

Total FMA-U/E scores improved significantly at 2 and 6 weeks after BoNT-A administration ($p = 0.003$, $p = 0.002$). There was no significant difference between the score at 12 weeks after administration and the score before administration. Subscale A (shoulder/elbow/forearm) scores improved significantly at 2 and 6 weeks after BoNT-A administration ($p = 0.003$, $p = 0.002$). Subscale B (wrist) scores tended to improve 2 weeks after BoNT-A administration ($p = 0.056$) and improved significantly 6 weeks after administration ($p = 0.009$). There was no improvement in the scores for Subscale C (hand) and Subscale D (coordination/speed) (Table 3).

Discussion

DAS, MAS, and FMA-U/E scores all improved significantly after BoNT-A treatment of upper limbs with spasticity. DAS assessment prior to BoNT-A administration revealed that approximately 60% of the patients exhibited disability in terms of hygiene, approximately 70% in terms of dressing and limb



(* $p < 0.05$, ** $p < 0.01$)

Figure 1. Changes in DAS.

Improvements in hygiene, dressing, and limb position were evident at 2 and 6 weeks after administration. There was no significant change in pain at any point after administration compared with before administration (Wilcoxon signed rank test with Bonferroni correction).

Table 2. Changes in MAS.

	Before			2 weeks			6 weeks			12 weeks		
	Median	25%	75%	Median	25%	75%	Median	25%	75%	Median	25%	75%
Shoulder adductors	1+	1	2	1**	1	1+	1+**	1	1+	1+	1	1+
Elbow flexors	2	1	2	1**	1	1+	1+**	1	1+	1+	1	2
Forearm pronators	1+	1	2	1**	0	1+	1**	0	1+	1*	1	1+
Wrist flexors	2	1+	3	1**	1	1+	1+**	1	1+	1+**	1	2
Finger PIP joint flexors	2	1+	2	1**	1	1+	1+**	1	1+	1+**	1	2
Thumb IP joint flexors	1+	1	1+	1**	0	1	1**	0	1+	1**	1	1+

Wilcoxon signed rank test with Bonferroni correction. * $p < 0.05$, ** $p < 0.01$. Percentages indicate percentile.

Table 3. Changes in FMA-U/E.

	Before	2 weeks	6 weeks	12 weeks
Total score	21.9±12.0	23.0±11.7**	23.9±11.3*	23.2±12.2
Subscale A score	15.4±7.0	16.6±7.0**	16.9±6.5**	16.0±6.9
Subscale B score	1.2±2.2	1.6±2.6	1.7±2.7*	1.5±2.5
Subscale C score	5.1±4.3	4.7±3.3	5.1±3.3	5.6±4.1
Subscale D score	0.2±0.7	0.2±0.7	0.2±0.9	0.2±0.8

Wilcoxon signed rank test with Bonferroni correction. Mean±SD. * $p < 0.05$, ** $p < 0.01$.

position, and approximately 30% in terms of pain. Among the studies that have provided a breakdown of DAS target items [4–10, 12, 14, 16, 17], a large proportion selected dressing or limb position as the targets, and only around 10% chose pain as the target. In this study, spasticity impaired the dressing actions and limb position in a large proportion of patients, and a few patients complained of spasticity-associated pain. With respect to severity, the DAS score was 3 (severe disability) for hygiene and limb position in over 20% of the cases. Pain was milder than the other three parameters. In terms of changes over time in spastic muscles after treatment with BoNT-A, the other three parameters exhibited significant improvement at 2 and 6 weeks after administration. The assessment of hygiene, one of the categories evaluated by DAS, includes not only active movements by the spastic upper limb but also whether or not the spastic hand can be washed using the hand on the unaffected side. In particular, severe paralysis in the functions of the peripheral areas of the upper limbs was apparent in our subjects in this study, as evidenced by the mean scores of 1.2 ± 2.2 for Subscale B and 5.1 ± 4.3 for Subscale C of the FMA-U/E evaluation prior to administration, making it highly likely that actions were performed by the unaffected hand. The improvements at 2 and 6 weeks after BoNT-A administration may therefore have been due to the alleviation of spasticity of the elbow, wrist, and finger flexor muscles, which would have both made it easier to hold the arm with the elbow extended during hand washing and improved the finger grip, making these movements easier. The limb position

parameter of the DAS evaluates the physical, mental, and social effects of abnormal positioning of the arm. Synergic movements of the flexor muscles predominate in severely spastic upper limbs, which frequently adopt the Wernicke-Mann posture with bent elbows and curled-up fingers. Alleviating spasticity of the flexor muscles of the upper limbs thus directly improves abnormal limb positioning. The dressing parameter of the DAS evaluates the ease of changing a dress or shirt and the effect of spasticity on the actions involved. Generally speaking, the actions entailed in passing the arm on one side through a sleeve when getting dressed require shoulder flexion and abduction and elbow extension movements. Passing the opposite arm through the other sleeve then requires abduction of the other arm, pulling the clothing with a sufficient degree of tension to enable the arm to pass smoothly through the sleeve. A patient with a spastic upper limb that tends to adopt an abnormally flexed position may thus have particular difficulty in performing dressing actions when changing clothes. Whether or not the patient is capable of voluntary movements of the shoulder and elbow may also constitute an important factor in the performance of these actions. BoNT-A administration may therefore have made dressing actions easier not only by reducing the spasticity of the upper limb extensor muscles, but also by improving the function of the central part of the upper limb expressed in Subscale A of the FMA-U/E. Increasing the number of opportunities for active movement of the upper limbs may also have improved the patients' abilities to perform dressing actions, leading to further

improvement at 6 weeks after administration compared with at 2 weeks. In terms of the active movement aspect, hand washing actions in hygiene may also be assumed to involve active movements of the wrist and fingers. However, as severe paralysis of the peripheral areas of the upper limbs was apparent in our study subjects before administration, with a mean score of 5.1 ± 4.3 on Subscale C of the FMA-U/E, as shown in Table 3, voluntary movements may not have increased because no improvement in motor function was achieved after the reduction in spasticity. Possible reasons for the absence of improvement in these three parameters at 12 weeks after administration may include spasticity of the elbow flexor muscles, which would have made it difficult to perform the actions involved in hand washing and passing the arms through sleeves while dressing that entail holding the elbow in an extended position. With respect to pain, approximately 70% of our subjects had a DAS score of 0 (no disability) for this parameter before administration while approximately 20% had a score of 1 (mild disability). No significant improvement was obtained because most of our subjects were already mild cases in this respect.

MAS scores, which express the severity of spasticity, all improved significantly 2 weeks and 6 weeks after the treatment of spastic muscles with BoNT-A. Our study thus showed a similar effect of BoNT-A administration in reducing spasticity to that already reported in other studies [21–23].

Total FMA-U/E scores and scores for Subscale A improved significantly 2 and 6 weeks after administration. On the other hand, scores for Subscale B improved significantly at 6 weeks, while exhibiting a tendency to improve at 2 weeks. Several previous studies have shown that FMA-UE scores are improved by concentrated practice after BoNT-A administration [24–27]. Takekawa et al. [24] reported that if patients were instructed to carry out exercises independently at home after administration, scores for Subscales A and B improved greatly 1, 3, and 6 months later, and scores for Subscale D also improved after 3 and 6 months. In the present study, we did not implement consistent instruction or intervention regarding rehabilitation or independent exercises after BoNT-A administration. The subjects, however, did continue to perform exercises after administration in settings such as outpatient rehabilitation at our hospital or another clinic, day care, and home rehabilitation visits, achieving significant improvement comparable with that seen in previous studies. In particular, the improvement in Subscale A, which expresses the function of the central part of the upper limbs, made a major contribution to the improvement in total score. This may have been because of significant improvements in the spasticity of the shoulder abductor, elbow flexor, and forearm pronator muscles, or because the subjects' score of 15.4 ± 7.0 for Subscale A of the FMA-U/E before administration

meant that at least some voluntary movement was possible. At 12 weeks after administration, the spasticity of the shoulder abductor and elbow flexor muscles was in the process of returning to its pre-administration level, eliminating the significant improvement in the Subscale A score and the total score. Subscale B was assessed with the elbow held at 90° flexion or completely extended. In the 12-week evaluation, this score must therefore have been affected at least somewhat by the increased spasticity of the elbow flexor muscles. Subscale C, which expresses the function of the peripheral parts of the upper limbs, exhibited more severe paralysis prior to BoNT-A administration. BoNT-A administration thus did not result in improved motor function due to reduced spasticity.

The limitations of this study include the fact that the muscles treated and the dose administered were determined by agreement between the doctor and patient, meaning that injection locations and doses were not necessarily consistent. Since the maximum dose that can be administered to the upper limb is 240 units in Japan, the dose may not have been sufficient. In addition, as injections were delivered to multiple muscles, we were unable to investigate which of the muscles that received injections contributed to improving the DAS scores. However, our results did demonstrate that approximately 60–70% of the patients with upper limb spasticity suffered from disabilities in hygiene, dressing, and limb position. Hygiene and limb position disabilities in particular were more severe. BoNT-A administration significantly improved difficulties in ADL as well as spasticity. Further studies are required to ascertain the specific causal relationship between muscle spasticity and ADL disabilities, as well as the improvement of these difficulties by multiple administration of BoNT-A.

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