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RESEARCH PAPER

The lowest effective dose of botulinum A toxin in adult patients with upper limb spasticity

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Abstract

Objective: To define the lowest effective dose of botulinum toxin type A (Dysport®) and safety in the treatment of adult patients with upper limb spasticity.

Design: This was a prospective, randomized, double-blind, dose-ranging study. Patients received either a placebo or one of three doses of Dysport® (350, 500, 1000 U) into five muscles of affected arm by anatomical and electromyography guidance. Efficacy was assessed periodically throughout the 6-month study period by the Modified Ashworth Scale (MAS), the Action Research Arm Test (ARA), the Barthel Index (BI) and the Visual Analogue Pain Scale (VAS).

Results: Fifty patients were recruited. The four study groups were comparable at baseline with respect to their demographical characteristics and severity of spasticity. All doses of Dysport® studied showed a significant reduction from baseline of muscle tone and pain compared to placebo. However, the effect of functional disability was best at a dose of 500 U and the peak improvement was at week 8 after injection. A dose of 1000 U Dysport produced such an excess degree of muscle weakening that the number of randomized patients was reduced to five. BI and ARA of all patients were decrease after injection. No other adverse event was considered related to the study medication.

Conclusion: This study suggests that treatment with Dysport® reduces muscle tone in adult patients with upper limb spasticity. The optimal dose for treatment of patients with residual voluntary movement in the upper limb appears to be 500 U.

Keywords: *Botulinum toxin, upper limb spasticity, adult patients*

Introduction

Despite considerable rehabilitation effort, the prognosis for recovery of upper limb function after stroke remains poor. Of patients with an initially paralyzed arm, only 4–5% regain their normal function, and up to 28% experience no recovery [1]. Because the function of the upper limbs is essential for many tasks of daily living, its impairment contributes to the reduction of the quality of life of the patients as well as increasing dependence. Even in patients with complete arm paralysis, spasticity can be an important contributor to disability, by causing pain or interfering with hygiene and dressing.

The current methods of treatment for muscle spasticity are unsatisfactory. Systemic antispasticity drugs are nonselective in their actions and may cause functional loss, e.g., inability to maintain sitting posture because of weakening of the trunk muscles. Paradoxically, in some patients these drugs reduce strength in normal muscles without having any effect on muscle spasticity [2]. Furthermore, the value of oral antispasticity drugs diminishes with prolonged use. Tolerance develops after a few months of treatment, and incremental increases in dosage are required to maintain the initial clinical response. The high doses required increase the incidence and severity of the adverse effects of the drugs.

An alternative strategy in the management of muscle spasticity is chemical neurolysis with alcohol or phenol. However, nerve blocks and motor point injection in the upper limbs cause skin sensory loss and dysesthesia, and their effect diminishes with repeated treatments [3]. The treatment is currently not recommended for upper limb spasticity when sensation is preserved. In recent years, botulinum toxin type A (BTA) has been shown to be an effective antispasticity agent [4–6]. BTA reversibly blocks the release of acetylcholine from the nerve endings at the

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neuromuscular junction [7]. Unlike alcohol and phenol nerve blocks, it has selective action on motor nerves without affecting sensory nerve conduction. Preserved perception is an integral part of maximizing motor recovery after stroke and therefore they are treatments that do not cause sensory disturbance, and hence have theoretical advantage over non-specific local treatments.

Open-labeled and placebo-controlled studies that investigate the use of BTA in patients with upper limb spasticity provide considerable evidence in support of it effectiveness in reducing dysfunctional muscle tone after stroke and brain injury [8–20].

Two preparations of BTA are currently available for intramuscular injection: the English formulation from Ipsen Ltd, DYSPORT®, and the American formulation, Botox®. The potency of these drugs is not therapeutically equivalent. A conversion factor of 3:1 to 4:1 is to be used when a patient is transferred from one formulation to the other. Since the smaller muscle mass and lower body mass index of Thai patients, and also the hot climate induces the extensibility of spastic muscles in Thailand, studies of BTA under various indications for Thai patients revealed that there is a potential for using lower doses of BTA than in foreign countries such as USA, Europe and Australia [21–26].

Objectives

1. To define the lowest effective dose of Dysport® in the treatment of upper limb spasticity in adult patients.
2. To define the onset and duration of Dysport® for decrement of muscle tone and muscle pain, increment of hand function and activities of daily living.
3. To define the clinical tolerance of Dysport® (safety finding).

Study design

This was a prospective, randomized, double-blind, dose-ranging clinical trial to define the lowest effective dose of Dysport® and safety in the treatment of upper limb spasticity of adult patients.

Ethics

The study was approved by the Ethics Committee of the Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. The study protocol was fully explained to eligible patients, and written informed consent was obtained from each subject before any study, specific assessments and injections were performed on them.

Materials and methods

Study population

Adult patients with spasticity who were consulted for treatments of upper limb spasticity at the Spastic and Dystonia Clinic, Department of Rehabilitation Medicine, King Chulalongkorn Memorial Hospital, were recruited into the study with the following inclusion and exclusion criteria. The study populations were randomized into four groups by a random table.

Patients were included in the study based on the following criteria: (1) male or female patient of any age above 15 years old; (2) any cause of spasticity (stroke, traumatic brain injury, spinal cord lesion, multiple sclerosis and degenerative diseases); (3) upper limb spasticity; (4) medically and neurologically stable; (5) subjects had no notable cognitive deficits, ambulate and competent of independent ADL; and (6) the subjects having received at least 6 months of rehabilitation therapy.

Exclusion criteria in the injection group were: (1) complete plegia (strength grade < 2 in target segments); (2) known hypersensitivity to any ingredient in the BTA preparation; (3) diagnosis of myasthenia gravis, Eaton Lambert syndrome, or amyotrophic lateral sclerosis (ALS); (4) uncontrolled systemic disease; (5) evidence of a fixed contracture in the target limb; (6) pregnancy, planned pregnancy or lactation; (7) current/previous surgery or phenol injections into target muscles; (8) concurrent use of aminoglycoside antibiotics; and (9) obvious atrophy of the muscles of target limb.

Study medication

Dysport® (Ipsen Ltd.; each vial contains 500 units (U) of *Clostridium* BTA in a sterile, vacuum-dried form), human albumin solution and lactose were studied. Depending on randomization, placebo or one of the three following doses of Dysport was administered: 150, 200 or 400 U for large muscles; and 50, 75 or 150 U for small muscles. Only upper limb muscles were injected, specifically, biceps brachii, flexor carpi ulnaris, flexor carpi radialis, flexor digitorum profundus, flexor digitorum superficialis. Biceps brachii were classified as large muscles and the others were as small muscles. The total dose and units of Dysport® injected at each site were as shown in Table I.

Injection technique

A 27-gauge Teflon-coated combination electromyography electrode/injection needle (Botox® injection needle; Allergan) was used both to locate the optimum injection site within each muscle, and to inject the toxin. The choice of injection site was

Table I. Units of Dysport® injected at each site.

Treatment Group	Total dose	Muscles				
		BB	FCU	FCR	FDP	FDS
I	0	0	0	0	0	0
II	350	150	50	50	50	50
III	500	200	75	75	75	75
IV	1000	400	150	150	150	150

BB, bicep brachii; FDP, flexor digitorum profundus; FDS, flexor digitorum superficialis; FCU, flexor capri ulnaris; and FCR, flexor capri radialis.

guided by anatomical knowledge of the location of the motor end plate of each muscle, established by standard guidelines [4]. All injections were done by the first author.

Concomitant medications

Concomitant medications that were considered necessary for the subject's welfare and did not interfere with the study were allowed to be used. Administration of all drugs and/or regimen alterations were carefully recorded.

Concomitant rehabilitation program

After injection, all patients were instructed to do stretching exercises of spastic injected muscles by the first author. They needed to do the exercises at home every day. They all had full program rehabilitation therapy of the upper extremities 3 days per week throughout the 6-month studied period.

Outcome measures

The effects of the treatment were assessed by the blinded observer as the following: (1) degree of spasticity using the Modified Ashworth Scale (MAS) [27]; (2) dexterity using the Action Research Arm test (ARA) [28]; (3) activities of daily living using the Barthel Index (BI) [29]; and (4) pain using the Visual Analogue Pain Scale (VAS) [30]. All patients were evaluated for MAS and VAS at baseline, and 2, 4, 8, 16 and 24 weeks after injections, and for ARA and BI at baseline, and 8 and 24 weeks after injections. Adverse events were evaluated based on spontaneous patient reports.

Statistical analysis

Mann–Whitney *U*-test was used for comparing changes in MAS at 8 weeks from baseline between placebo and Dysport® groups (significant change at $P < 0.05$). Mann–Whitney *U*-test with Bonferroni correction was used for comparing changes in MAS at 8 weeks from baseline between three doses of Dysport® group (significant change at $P < 0.05$).

One-way ANOVA was used for comparing changes in ARA, BI and VAS between placebo and Dysport® groups (significant change at $P < 0.05$). One-way ANOVA with Bonferroni correction was used for comparing changes in ARA, BI and VAS between three doses of Dysport® groups (significant change at $P < 0.05$).

Results

A total of 50 patients were recruited and randomized into the following groups: placebo, $n = 15$; Dysport® 350 U, $n = 15$; Dysport® 500 U, $n = 15$; Dysport® 1,000 U, $n = 5$. At first, we planned to recruit 15 patients to each group. However, after injection of 1,000 U Dysport® in five patients, all of them complained of too much weakness of their arms. The global assessment of function by BI and dexterity by ARA was decreased after injection of 1000 U Dysport®. So we decided to stop recruitment into the 1,000 U Dysport® group. The demographic data and disease characteristics of all the study groups were similar at baseline, as shown in Table II.

Efficacy

Mean MAS dropped within 2 weeks of treatment, approached the lowest at week 8 and then gradually increased throughout the 6-month studied period in placebo, and 350 and 500 U Dysport® groups. Mean MAS dropped within 2 weeks of treatment, approached zero at weeks 2–8 and then gradually increased throughout the 6-month studied period in the 1,000 U Dysport® group, as shown in Figure 1.

Mean ARA and BI increased during the first 8 weeks and then became rather stable throughout the 6-month study period in the 350 and 500 U Dysport® groups. Mean ARA and BI were rather stable throughout the 6-month study period in the placebo group. Mean ARA and BI were decreased in the first 8 weeks and then became rather stable

Table II. Demographic characteristics and disease characteristics at baseline.

		Dysport®		
	Placebo ($n = 15$)	350 U ($n = 15$)	500 U ($n = 15$)	1000 U ($n = 15$)
Age, mean (SD), range (years)	55.2 (8.94) 39–68	46.53 (8.53) 35–66	53 (18.69) 37–87	59.85 (9.15) 40–70
Sex				
Male	7	8	8	3
Female	8	7	7	2
Body weight, mean(SD), range (kg)	58.04 (6.41) 45–68	61.27 (4.67) 52–68	59.8 (6.79) 45–70	58.4 (9.81) 44–69
Etiology:				
Ischemic stroke	8	9	8	3
Hemorrhagic stroke	6	6	6	2
Cerebral embolism	1	0	1	0
Durations since onset of stroke				
Mean (SD),	8.5 (0.8)	7.9 (0.9)	8.4 (0.7)	8.7 (0.4)
Range (months)	6–12	6–11	6–12	6–12
Hemiparetic arm:				
Dominant	7	9	8	3
Non-dominant	8	6	7	2
Severity of spasticity by MAS	4	4	4	4

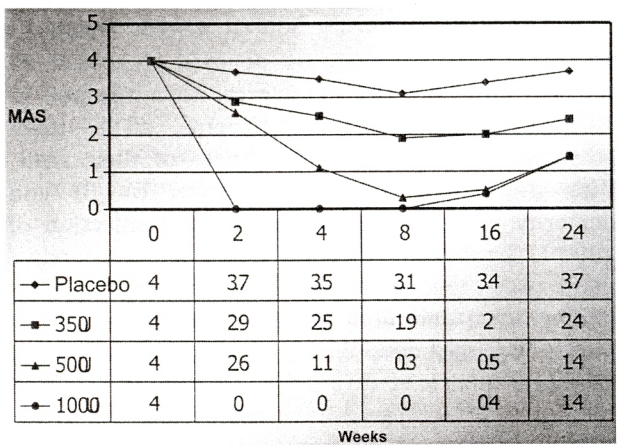

Figure 1. MAS at different times in each group.

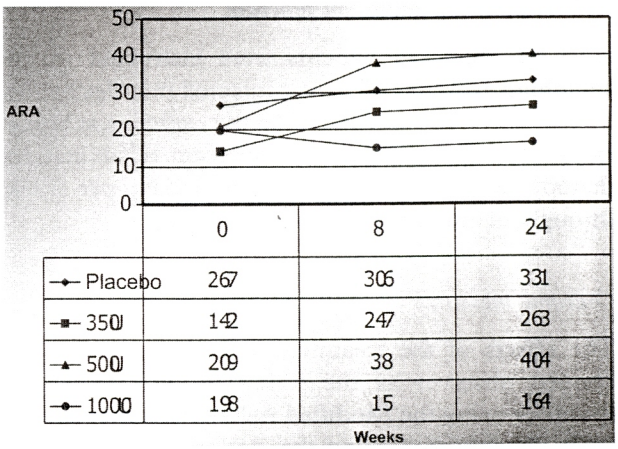

Figure 2. ARA at different times in each group.

throughout the 6-month study period in the 1000 U Dysport® group, as shown in Figures 2 and 3.

Mean VAS dropped within 2 weeks of treatment, approached the lowest at week 8 and then was rather stable throughout the 6-month study period in the 350, 500 and 1000 U Dysport® groups. Mean VAS dropped 50% within 2 weeks of treatment, approached nearly zero at week 4 and throughout the 6-month study period in the 1,000 U Dysport® group, as shown in Figure 4.

All three doses of Dysport® resulted in significant reduction in the MAS score at week 8, compared with placebo. The number of patients who had improvement of the MAS ≥ 1 was significantly higher in all three Dysport® groups than in the placebo group by the Mann–Whitney *U*-test at

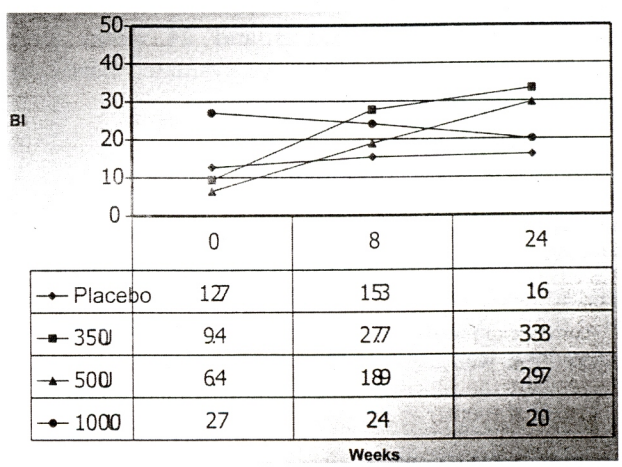

Figure 3. BI at different times in each group.

$P < 0.05$. The change of MAS in the 500 and 1000 U Dysport® groups was significantly higher than in the 350 U Dysport® group by the Mann–Whitney *U*-test with Bonferroni correction at $P < 0.05$, as shown in Table III.

The 500 U Dysport® group had a statistically significant increase in ARA at weeks 8 and 24 compared to the placebo group by one-way ANOVA at $P < 0.05$. The 1000 U Dysport® group had a statistically significant decrease in ARA at weeks 8 and 24 compared to the placebo group by one-way ANOVA at $P < 0.05$, as shown in Table IV.

The 350 and 500 U Dysport® groups had a statistically significant increase in BI at weeks 8 and 24 compared to the placebo group by one-way ANOVA at $P < 0.05$. However, the 500 U Dysport® group had a statistically significantly higher change in BI at weeks 8 and 24 compared to the 350 U Dysport® group by one-way ANOVA with Bonferroni correction at $P < 0.05$, as shown in Table V.

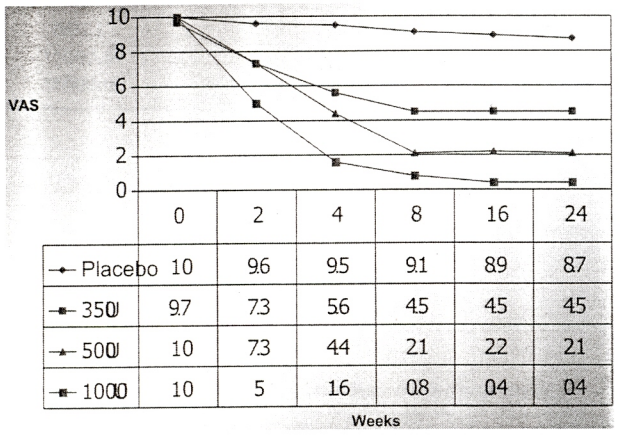

Figure 4. VAS at different times in each group.

All three Dysport® groups had a statistically significant decrease in VAS at weeks 8 and 24 compared to the placebo group by one-way ANOVA at $P < 0.05$. However, the 500 and 1000 U Dysport® groups had a statistically significant decrease in VAS in BI at weeks 8 and 24 compared to the 350 U Dysport® group by one-way ANOVA with Bonferroni correction at $P < 0.05$, as shown in Table VI.

Safety

Adverse events were reported by 12 patients in the four treatment groups, i.e., 24% of the study population. No fatal, life-threatening, or incapacitating adverse events related to the study medication were reported or observed. Overall, five of five patients (100%) reported too much weakness ($n = 5$); and one of five patients (20%) reported epileptic seizures ($n = 1$) in the 1000 U Dysport® group. Four of 15 patients (26.67 %) in the placebo group reported epileptic seizures ($n = 2$), accidental injury ($n = 1$), and urinary tract infection ($n = 1$). Two of 15 patients (13.33 %) in the 350 U Dysport® group reported epileptic seizures ($n = 2$). One of 15 patients (6.67%) in the 500 U Dysport® group reported epileptic seizures ($n = 1$). None of the adverse events, except too much weakness, were considered to be related to the study medication.

Discussion

In the first randomized, double-blinded, placebo-controlled trial addressing spasticity caused by stroke, Simpson et al. [6] studied the use of BTA in 39 patients with severe upper extremity spasticity. Three groups of patients, all with post-stroke duration of more than 6 months, underwent injection of either placebo, 75, 150 or 300 U of Botox®

Table III. Summary of best change at week 8 from baseline in the MAS.

		Dysport®		
Change in MAS from baseline	Placebo ($n = 15$)	350 U ($n = 15$)	500 U ($n = 15$)	1000 U ($n = 5$)
Decrease of 4	0	3 (20%)	13 (86.7%)	5 (100%)
Decrease of 3	0	0	5(33.3%)	0
Decrease of 2	0	7(46.7%)	2(13.3%)	0
Decrease of 1	13(86.7%)	5(33.3%)	0	0
No change	2(13.3%)	0	0	0
Increase of 1	0	0	0	0
P (compare to placebo)		0.000*	0.000*	0.000*
P (350 U & 500U)			0.000**	
P (500 U & 1000U)				0.402
P (350 U & 1000U)				0.005**

* *P* value by Mann–Whitney *U*-test, significant at $P < 0.05$.

** *P* value by Mann–Whitney *U*-test with Bonferroni correction, significant at $P < 0.05$.

Table IV. Change in Action Research arm Test (ARA) at different times from baseline.

	Treatment group	Mean (SD) Range (Min–Max)	95% CI	Comparison with placebo		P
				Mean	95% CI	
Change in ARA at week 8	Placebo	7.87 (7.42) 1–25	3.76, 11.98			
	350 U	13.93 (8.60) 1–25	9.17, 18.69	6.07	−2.53, 14.48	0.318
	500 U	17.13 (10.01) 5–43	11.59, 22.68	9.27	0.85, 17.69	0.024*
	1000 U	−4.8 (1.3) (−6)–(−3)	−6.41, −3.18	− 12.67	−24.57, −0.76	0.031*
P (350 & 500U)						1.000
P (500 & 1000U)						0.000**
P (350 & 1000U)						0.000**
Change in ARA at week 24	Placebo	9.53 (8.00) 1–27	5.10, 13.97			
	350 U	16.47 (9.86) 1–29	11.01, 21.93	6.93	−1.92, 15.79	0.217
	500 U	19.53 (9.61) 6–39	14.21, 24.86	10.00	1.14, 18.86	0.019*
	1000 U	−3.40 (1.34) (−5)–(−2)	−5.07, −1.73	−12.93	−25.46, −0.41	0.039*
P (350 & 500U)						1.000
P (500 & 1000U)						0.000**
P (350 & 1000U)						0.000**

* *P* value by one-way ANOVA, significant at $P < 0.05$.

Table V. Change in Barthel Index (BI) at different times from baseline.

	Treatment group	Mean (SD) Range (Min-Max)	95% CI	Comparision with placebo		P
				Mean	95%CI	
Change in I at week 8	Placebo	2.67 (2.58) 0–5	1.23, 4.10			
	350 U	9.67 (7.43) 0–25	5.55, 13.78	7.00	1.12, 12.88	0.012*
	500 U	23.33 (6.99) 10–35	19.46, 27.208	20.67	14.78, 26.55	0.000*
	1000 U	−1.00 (2.24) (−5)–(0)	−3.77, 1.78	−3.67	−11.98, 4.65	1.000
P (350 & 500 U)						0.000**
P (500 U&1000 U)						0.000**
P (350 U&1000 U)						0.000**
Change in BI at week 24	Placebo	3.33 (2.44) 0–5	1.98, 4.68			
	350 U	17.33 (13.21) 0–40	10.02, 24.643	14.00	5.68, 22.31	0.000*
	500 U	31.67 (6.45) 20–45	28.09, 35.24	28.33	20.01, 36.65	0.000*
	1000 U	−2.00 (2.74) (−5)–(0)	−5.40, 1.40	−5.33	−17.09, 6.43	
P (350 & 500 U)						0.000*
P (500 & 1000 U)						0.000*
P (350 & 1000 U)						0.000*

*P value by one-way ANOVA, significant at $P < 0.05$.

** *P*-value by one-way ANOVA with Bonferroni correction, significant at $P < 0.05$.

Table VI. Change in Visual Analogue Pain Scale (VAS) at different times from baseline.

	Treatment group	Mean (SD) Range (Min-Max)	95% CI	Comparison with Placebo		*P*
				Mean	95%CI	
Change in VAS at week 8	Placebo	0.87 (0.64) 0–2	0.51, 1.22			
	350 U	5.27 (3.06) 2–10	3.57, 6.96	4.40	2.08, 6.71	0.000*
	500 U	7.93 (2.73) 2–10	6.35, 9.50	7.06	4.70, 9.42	0.000*
	1000 U	9.20 (1.10) 8–10	7.83, 10.56	8.33	5.05, 11.61	0.000*
P (350 & 500 U)						0.019**
P (500 & 1000 U)						0.011**
P (350 & 1000 U)						1.000
Change in VAS at week 24	Placebo	1.27 (0.88) 0–2	0.78, 1.76			
	350 U	5.27 (3.06) 2–10	3.57, 6.96	4.00	1.68, 6.32	0.000*
	500 U	7.86 (2.68) 2–10	6.31, 9.41	6.59	4.23, 8.95	0.000*
	1000 U	9.60 (0.89) 8–10	8.49, 10.71	8.33	5.05, 11.61	0.000*
P (350 & 500 U)						0.025**
P (500 & 1000 U)						0.004**
P (350 & 1000 U)						0.920**

*P value by one-way ANOVA, significant at $P < 0.05$.
** P value by one-way ANOVA with Bonferroni correction, significant at $P < 0.05$.

into biceps brachii, flexor carpi radialis, and flexor carpi ulnaris. Significant physician and patient global assessment scales were also reported. Treatment with the highest dose resulted in a significant decrease in muscle tone for up to 6 weeks after injection; however, no significant differences were observed between placebo and treatment for motor function, pain, caregiver dependency, and competence in daily activities.

Favorable reductions in muscle tone were also reported among randomized controlled trials published later, including three reported cases in the previous year. Bakheit et al. [11] described the results of a multicenter, randomized, placebo-controlled, dose-ranging study among patients with upper extremity spasticity caused by stroke. The 83 recruited subjects were placed into four groups, which received either placebo or doses of Dysport® (500, 1000 or 1500 U) divided into five muscles of the affected arm. All doses of BTA showed a significant reduction of muscle tone compared with placebo. The effect on functional disability was not statistically significant, however, and was best at the dose of 1000 U.

Bhakta *et al.* [16] described more favorable results on functional outcome among patients treated in another recent randomized, placebo-controlled trial. The investigators specifically explored the relationship between reduction in spasticity and response in measures of disability and caregiver burden. Forty patients with BTA (Dysport®) ($n = 20$) or placebo ($n = 20$), divided between elbow, wrist, and finger flexors. Spasticity improved in the forearm flexor for 12 weeks, but lasted only 2 weeks in the elbow flexors. Disability and caregiver burden ratings improved among patients who were treated with BTA. However, the relationship between the measures of function and spasticity was not straightforward.

In the largest multicenter randomized trial completed to date, Brashear et al. [9] recently presented preliminary results of a study addressing the efficacy of BTA (Botox®) on upper extremity spasticity caused by stroke. Of the 126 patients randomized either to injection of BTA or placebo, 122 completed the study. Outcome measures included the modified Ashworth scale, physician and caregiver ratings of outcome, and instruments measuring outcome in four defined domains of function, including a patient-identified primary goal of therapy. Not surprisingly, BTA injection improved distal upper extremity spasticity at all post-injection visits, with peak effect noted at week 4. Caregiver and physician ratings of response also showed significant improvement at all periods assessed. When compared with the placebo group, patient-identified goals of therapy improved at all time points among patients injected with BTA. Prospectively identified measures of

disability significantly correlated with caregiver and physician response ratings and spasticity reduction. These preliminary data again confirm the favorable response of BTA on focal dysfunctional spasticity. Moreover, they suggest that careful study design, including measures for patient-identified goals of treatment, facilitates evaluation of the functional impact of focal spasticity reduction.

The results of this study indicate that Dysport® reduces upper limb spasticity in adult patients as previous studies [8–20]. There were no Dysport®-related serious adverse effects nor changes in safety measures. This indicated that Dysport® injections were well tolerated.

The primary efficacy measure in this study was measurement of muscle tone of the elbow, wrist flexors and finger flexors using MAS. A change of 1 point on MAS is considered clinically significant. Patients in all 350, 500 and 1000 U Dysport® groups showed both a clinically and statistically significant reduction of muscle tone. The peak effect of 350 and 500 U Dysport® groups occurred at 8 weeks post injection. MAS of all patients in the 1000 U Dysport® groups were zero at the beginning of 2 weeks and all patients showed excessive weakening of the injected muscles. There was no consistent spread of effect (due to diffusion of toxin or to a synergistic effect) to adjacent non-injected muscle groups as measured by reduction of muscle tone or change in strength.

The changes in ARA, BI and VAS correlated well with the results of the MAS. The changes showed peak improvement at week 8 post injection in the 350 and 500 U Dysport® groups. The change showed peaks of improvement in MAS and VAS and peak of decrement of functional ability by ARA and BI at week 2 post injection in the 1000 U Dysport® group. At a dose of 1000 U, the range of active movement was sometimes reduced, probably because of excessive weakening of the injected muscles.

The changes in ARA and BI revealed statistically significantly best improvement in the 500 U Dysport® group and the peak improvement was at week 8 post injection. A dose of 1000 U and placebo groups showed no statistically significant improvement in ARA and BI.

Regarding the measurement of all outcomes, the optimal dose of Dysport® for the treatment of patients with residual voluntary movement in the upper limb appears to be 500 U. The findings of Botox® (Allergan Inc.) for MAS 4 in adult spastic patients in Thailand [26] were: biceps 75 units; flexor carpi radialis 25 units; flexor carpi ulnaris 25 units; flexor digitorum profundus 25 units; and flexor digitorum superficialis 25 units [26]; all these data were based on the assumption of a Dysport®/Botox® dose conversion ration of 3:1. In this dose ratio, the two products appear to have the same therapeutic equivalence.

The optimal dose of Dysport® found in this study is 1/2 of the recommended dose. In Thailand, Suputtitada et al. reported the efficacy and safety of Botox® in cerebral palsy, stroke patients, writer's cramp, hemifacial spasm, cervical dystonia and chronic myofascial pain syndrome [21–26]. All patients used low-dose regimen: half to two-thirds of the recommended dose. The possible explanations were: (1) the smaller muscle mass of the Thai population; (2) the hot climate in Thailand facilitates extensibility of the spastic muscle; (3) the concomitant rehabilitation program after injection; and (4) the inclusion criteria of subjects who had no notable cognitive deficits and were able to use their upper limbs after injection. Several papers focus on methods to improve the results of treatment with BTA in spastic disorders: electrical stimulation improves the action of BTA in patients with leg spasticity, hemiparesis and in those presenting with arm flexor spasticity following stroke [31–33]. Muscle stretching may improve the therapeutic effect of BTA [34]. Automatic EMG guidance may improve the result of treatment with BTA [35]. Therefore, in Thailand, we use a lower dose than in the USA, Europe and Australia.

Conclusion

This study suggests that treatment with Dysport® reduces muscle tone in adult patients with upper limb spasticity. The optimal dose for the treatment of patients with residual voluntary movement in the upper limb appears to be 500 U.

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