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SHORT COMMUNICATION

A SINGLE-BLINDED, RANDOMIZED PILOT STUDY OF BOTULINUM TOXIN TYPE A COMBINED WITH NON-PHARMACOLOGICAL TREATMENT FOR SPASTIC FOOT*

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Objective: **To explore the effect of treatment after botulinum toxin type A combined with treatments for the spastic foot.**
Design: **Single-blind, randomized trial, with 3-month follow-up.**
Subjects: **Twenty-three chronic hemiplegic adult patients with spastic equinus foot.**
Methods: **Following botulinum toxin type A injection at the medial and lateral gastrocnemius, patients were assigned randomly to 3 groups, and treated with taping, electrical stimulation or stretching. They were evaluated before treatment (t0), and at 10 (t1), 20 (t2) and 90 (t3) days after treatment. Outcome measures were: Modified Ashworth Scale; passive range of motion at the ankle; measurement of muscle action potential at the gastrocnemius medialis; and measurement of maximum ankle dorsiflexion angle in stance using gait analysis.**
Results: **The group treated with electrical stimulation performed better at t1 on the Modified Ashworth Scale. The taping and electrical stimulation groups performed better in all outcome measures at t3. The taping group performed better mainly for maximum ankle dorsiflexion angle in stance. The stretching group showed a less durable result, with some worsening at the t3 evaluation compared with the assessment performed before treatment.**
Conclusions: **This pilot study indicates that combining botulinum toxin type A administration for the ankle plantar flexors with taping and electrical stimulation might be beneficial.**

Key words: hemiplegia, botulinum toxin type A, muscle spasticity, therapeutic electrical stimulation, muscle stretching exercises.

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INTRODUCTION

Spasticity of the plantar flexors can lead to equinovarus foot, provoking walking impairment in stroke patients (1). Botulinum toxin type A (BoNT-X) has proven effective in treating post-stroke focal spasticity (2). To enhance the effects of BoNT-X, various rehabilitative techniques have been utilized, including stretching (3), functional electrical stimulation (4), taping (5) and therapeutic exercise (6). Even if the association of BoNT-X with rehabilitative treatments is accepted (7), there is no agreement as to which treatment is the most effective in the early phase after its administration. Moreover, there is no evidence that any one treatment is better than another for lower limb spasticity in patients after stroke. The objective of this pilot study was to determine which would be the most effective rehabilitative option after BoNT-X administration at the ankle plantar flexors, among stretching, electrical stimulation and taping.

MATERIAL AND METHODS

Patients were enrolled among those referred to our gait analysis laboratory. Inclusion criteria were: (*i*) hemiplegia after ischaemic or haemorrhagic stroke documented by a computerized tomography (CT) scan and/or available case history (subarachnoidal haemorrhage excluded); (*ii*) time from stroke at least 6 months; (*iii*) equinovarus foot with spastic hypertonia of gastrocnemii (*ii*) graded at least 1+ with the Modified Ashworth Scale (MAS) (8); (*iv*) ability to walk without assistance; (*v*) last BoNT-X treatment and/or any rehabilitative treatment at least 3 months prior to access to the laboratory. Exclusion criteria were: (*i*) fixed contractures and/or bony deformities at the ankle; (*ii*) cognitive impairments limiting the ability to understand motor tasks required during treatment; (*iii*) concomitant progressive central nervous system (CNS) disorders, peripheral nervous system disorders/myopathies; (*iv*) previous surgery of the plantar flexor muscles on the affected side. Voluntary and spontaneous electromyographic (EMG) activity was studied in all patients and those with evidence of active denervation were excluded. Toxin administration was considered appropriate where co-contraction and/or continuous resting activity and/or stretch-induced EMG activity on the gastrocnemii was recorded. BoNT-X (Dysport®, Ipsen, Slough, UK), 500 IU diluted with 1.25 ml of saline 0.9%, was injected into the lateral and medial head of the gastrocnemius of the affected side, according to clinical and EMG findings. Depending on spastic hypertonia grade and muscle size, the BoNT-X dose was adjusted in a range between 150 and 250 IU for each muscle head. The 2 muscle heads received the same dose of BoNT-X. After inoculation, patients were assigned to 1 of 3 treatment groups using a simple software-generated randomization scheme (9).

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Group 1: electrical stimulation and stretching (ES)

Patients received electrical stimulation (5-Hz, rectangular biphasic balanced current) of the injected muscles for 5 days, 30 min twice a day. Intensity was adjusted to the patient's tolerance. Each electrical stimulation session was followed by stretching of the calf muscles for 20 min.

Group 2: taping

Patients were treated with adhesive taping at the ankle and thigh to stretch the injected muscles. Taping was maintained for 5 days, and was checked and rearranged daily by a trained physical therapist. Taping was checked daily and the strips were pulled to reach the desired position, i.e. full elongation of the spastic muscle.

Group 3: stretching

The patients in this group were submitted to a programme of 30 min stretching of the calf muscles twice a day for 7 days; the patients were assisted by a physiotherapist.

Clinical and instrumental evaluations were carried out prior to BoNT-X administration (t0), and 10 (t1), 20 (t2) and 90 days (t3) after injection. Clinical assessments, gait analysis data and neurophysiological data collection were performed by the authors blinded to the subsequent rehabilitative regimen. BoNT-X injections were always administered by the same author, who was aware of the allocation arm. At each assessment, the following variables were measured: (*i*) spasticity of the injected muscles using MAS; (*ii*) passive range of motion (PROM) of the ankle joint, measured in all patients with the knee fully extended using a hand-held goniometer. We arbitrarily decided the sensitivity of the measurement in 5 degrees; (*iii*) measurement of motor action potential (MAP) of the treated medial gastrocnemius. The distance between the stimulation and registration points was maintained constant for all evaluations. The MAP percentage reduction was considered with respect to the t0 value; (*iv*) kinematic evaluation of ankle sagittal plane movement of the paretic side during walking (10). The angle of maximal dorsiflexion during the stance phase was considered. Regarding evaluations (*ii*) and (*iv*), we designated the dorsiflexion angle as positive and the plantar flexion angle as negative, considering the neutral position of the joint as 0 degrees. Group homogeneity was evaluated with the Kruskal-Wallis test. Differences between single variable measurements in each group were evaluated with Wilcoxon's signed-rank test at t1, t2 and t3. Differences between groups were evaluated with the Mann-Whitney *U* test. For statistical purposes, a MAS score "1" was considered as 1, a MAS score "1 +" as 2, and so on until 5 (11). Data are presented with the indication of ± 1 standard deviation (SD). An alpha error value of 0.05 was chosen.

RESULTS

Twenty-three hemiplegic patients with equinovarus foot deformity were enrolled in the study from a group of 84 patients with hemiplegia evaluated from December 2005 to November 2006. None of the enrolled patients had evidence of active denervation on EMG evaluation. Patient characteristics and allocation arm are summarized in Table I. Age and BoNT-X dose administered were well-matched between groups ($p > 0.5$). At follow-up, the following differences were found (Table II):

- At t1 all groups performed significantly better with respect to PROM, neurophysiological and gait analysis data. MAS scores were significantly improved only in the ES group.
- At t2 all groups performed significantly better than t0 for all evaluations, except for PROM measurements in the stretching group. Inter-group comparisons showed that the ES group improved significantly more than the stretching group on MAS scores and MAP reduction, while the taping group showed significantly lower MAS scores than the stretching group.
- At t3 the ES and taping groups performed significantly better on MAS scores and MAP reduction compared with t0 values. The taping group still showed meaningful improvements in gait analysis data compared with t0. No differences from t0 measurements were seen for all groups with respect to PROM. Interestingly, gait analysis data in the stretching group were worse than those measured at t0.

DISCUSSION

Our data support the hypothesis that the application of different treatments after BoNT-X administration could influence outcome in both the short- and medium-term. Patients treated with ES and taping performed better. At t1 all evaluated parameters improved more in the ES group than in the other groups. Patients in the ES and taping groups showed a greater and earlier reduction of MAP compared with patients in the stretching group. This result suggests a greater denervation induced by BoNT-X, consistent with an increased uptake of the toxin. Some authors reported a beneficial effect of electrical stimulation after BoNT-X on upper (4) and lower limb spasticity (12). In the present study, at 3 months' follow-up, patients in the taping group showed a greater improvement in all parameters than did patients in the other treatment groups, especially for the ankle dorsiflexion angle in stance. This is especially relevant because ankle dorsiflexion was measured during walking. One possible explanation is that prolonged stretching of a muscle by taping could lead to enhanced in-

Table I. *Patients characteristics at inclusion, according to allocation*

	ES *n* = 8	Taping *n* = 8	Stretching *n* = 7
Male, *n*	5	3	5
Hemiplegia, right/left, *n*	5/3	4/4	3/4
Age, years, mean (SD)	64.75 (7.36)	60.37 (12.75)	61.29 (5.74)
Time since stroke, months, mean (SD)	17.12 (6.49)	20.75 (13.68)	15.28 (8.85)
BoNT-A dose per muscle, IU, mean (SD)	193.75 (32.04)	200 (0)	192.86 (18.90)

ES: electrical stimulation group; taping: taping group; stretching: stretching group; IU: units; SD: standard deviation.

Table II. *Outcome measures at inclusion and follow-up (n = 23)*

		T0 Mean (SD)	T1 Mean (SD)	T2 Mean (SD)	T3 Mean (SD)
MAS	ES	3.75 (0.46)	2.5* (0.93)	1.62*† (0.52)	2.37* (0.52)
	Taping	3.62 (0.52)	2.87 (0.99)	1.75*‡ (0.71)	2.5* (0.53)
	Stretching	3.71 (0.49)	3.14 (0.9)	2.57* (0.53)	3.43 (0.79)
PROM, degrees	ES	–1.25 (2.31)	2.5* (3.78)	7.5* (2.67)	0 (2.67)
	Taping	–6.25 (6.94)	–1.88* (6.51)	–0.63* (6.78)	–5 (3.78)
	Stretching	–2.14 (2.67)	1.43* (2.44)	1.43 (3.78)	–2.14 (2.67)
Max. DF Stance Phase, degrees	ES	6.4 (5.08)	8.58* (4.28)	9.45* (4.68)	8.04 (3.97)
	Taping	5.92 (4.53)	7.72* (4.38)	7.94* (3.89)	7.31* (3.84)
	Stretching	9.49 (5.05)	10.92* (3.73)	11.37* (3.87)	8.39 (5.51)
MAP, % MAP reduction vs t0	ES	–	–27.56* (14.99)	33.94*† (18.59)	–42.13* (9.94)
	Taping	–	–39.07* (26.55)	–46.94* (27.03)	–46.5* (33.27)
	Stretching	–	–33.66* (29.71)	–54.61* (15.39)	–5.28 (14.3)

*$p < 0.05$; †$p < 0.05$ ES vs stretching; ‡$p < 0.05$ taping vs stretching.
MAS: Modified Ashworth Scale; PROM: passive range of motion; Max. DF Stance Phase: angle of maximal dorsiflexion during stance phase; MAP: motor action potential; ES: electrical stimulation group; Taping: taping group; Stretching: stretching group; SD: standard deviation; T0: before treatment; T1: 10 days after treatment, T2: 20 days after treatment; T3: 90 days after treatment.

ternalization of BoNT-X (producing muscular activation by elicitation of the tonic stretch reflex) and a positive action on the rheological properties of spastic muscles even in the short-term (13).

The stretching group showed the least marked modifications for all parameters. Moreover, the angle of maximal dorsiflexion at the ankle in the stance phase had worsened with respect to baseline. This finding is particularly noteworthy because stretching is a commonly prescribed treatment after BoNT-X (3). A possible explanation for the poorer result of stretching compared with taping is the shorter duration of stretching. This hypothesis has been put forward previously (14).

The major limitation of our study is its small sample size, although this is common to other studies performed on this subject (5, 12). However, the single-blind randomized design of the study reduces the possibility of operator bias. Moreover, 3 out of 4 evaluated measures were instrumental and therefore less prone to inter-observer variability, even if PROM assessment is subject to some tolerance. Since we assessed patients once before injecting BoNT-A, we can not exclude a bias caused by spontaneous amelioration.

However, to our knowledge there is no evidence in the literature of a placebo effect on kinematic and neurophysiological measurements.

Since we assessed patients once before injecting BoNT-X, we cannot exclude a bias caused by spontaneous amelioration. However, the mean time since stroke was greater than one year in our patients, which is considered reasonable to exclude meaningful spontaneous improvements. Moreover, modifications were observed within a time-span consistent with those expected after BoNT-X administration.

Further studies on a larger number of patients are required to provide more reliable and conclusive results and to compare different treatment strategies with extended outcome analysis in order to determine the best treatment option after BoNT-X injection.

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