

A single group, pretest-posttest clinical trial for the effects of botulinum toxin injection using dual guidance into the upper extremity muscles for the treatment of focal spasticity in patients with chronic stroke

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Abstract

Objective: This study aimed to determine if ultrasonography and electrical muscle stimulation-guided botulinum toxin injection into the upper extremity muscles increases the efficacy of the treatment of focal spasticity in patients with chronic stroke.

Materials and Methods: This study included 22 chronic hemiplegic stroke patients with grade 2 and 3 spasticity in the upper extremity muscles, based on the Modified Ashworth Scale. The study hypothesis was that ultrasonography and electrical muscle stimulation-guided botulinum toxin injection would increase the efficacy of the treatment of spasticity. The Modified Ashworth Scale, Tardieu Scale, Barthel Index and Fugl-Meyer Motor Assessment Scale were administered at baseline, and at 2 weeks and 2 months post treatment.

Results: All parameters were improved significantly at 2 weeks post treatment, as compared to baseline, and the observed improvement persisted at 2 months post treatment ($P < 0.05$).

Conclusion: Ultrasonography and electrical muscle stimulation-guided botulinum toxin injection significantly improved spasticity and functional recovery in chronic stroke patients with upper extremity spasticity.

Keywords: spasticity, botulinum toxin, injection, ultrasonography, stimulation

Introduction

Spasticity is a cause of disability in 38% of stroke patients during the first year post stroke (1). Spasticity can negatively affect daily activities and a patient's physical appearance, balance, and gait pattern (2). Botulinum toxin (BTX) injection is a safe, effective, and commonly used method for the treatment of focal and multifocal spasticity. Correct muscle group selection and injection technique are the primary factors associated with successful treatment. BTX is reported to be most effective when injected correctly and into the deep-seated motor end plates in muscles (3). Intramuscular BTX injection can be performed using several types of guidance, including manual needle placement (MNP), electromyography (EMG), electrical muscle stimulation (EMS), and ultrasonography (US). EMS- or US-guided injection is recommended, especially for deep-seated and small muscles (4-6). The present study aimed to determine if US and EMS-guided BTX injection into the upper extremity muscles increases the efficacy of the treatment of focal spasticity in patients with chronic stroke.

Material and Methods

The study included 22 chronic hemiplegic stroke patients with grade 2 and 3 spasticity in upper extremity muscles, based on the Modified Ashworth Scale (MAS). Inclusion criteria were as follows: Spastic hemiparesis secondary to ischemic or hemorrhagic stroke; time from stroke onset at least 6 months; aged 20-75 years; grade 2 or 3 spasticity of the all affected upper extremity muscles, including: the biceps, pronator teres, flexor carpi radialis, flexor carpi ulnaris, flexor digitorum superficialis and flexor digitorum profundus, based on MAS. Exclusion criteria were as follows: Fixed contractures (tone grade 4, according to MAS); tumor or severe trauma in the affected arm; ongoing treatment with oral anti-spastic medication; BTX treatment within 3 months of the study start date; history of surgical treatment of fixed contractures affecting the arm; pregnancy; lactation; formation of neutralizing antibodies against BTX (previous 2 injections ineffective). All the patients were evaluated as 1 group. All the patients provided written informed consent and the study protocol was approved by the local Ethics Committee.

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Procedures

Abobotulinumtoxin-A was injected (Dysport, Ipsen, France) (500 U diluted with 2 mL of 0.9% saline) into all of the affected upper extremity muscles including: the biceps, pronator teres, flexor carpi radialis, flexor carpi ulnaris, flexor digitorum superficialis and flexor digitorum profundus. The dose was 125 U for all muscles on the purpose of standardization. Patients were placed in the supine position, the shoulder was abducted, the elbow was extended, and the forearm was placed in supination. The injection area was covered with sterile drape, and skin antisepsis was provided. Firstly, each targeted muscle was observed via US, using an M-Turbo system (Sonosite, USA) with a linear transducer (scanning frequency 7-12 MHz) and sterile gel. The transducer was positioned for the transverse view, perpendicular to the arm and forearm surface. A 25-G EMS needle (50 × 0.5 mm, hypodermic, single use, Teflon coated, Technomed Europe, Netherlands) was inserted into the targeted muscle at a 30° angle to the transducer via the outline method under US guidance. The depth of the needle tip inside each target muscle was determined via the gentle and reciprocating movements of the needle. After confirming that the needle was in the target muscle, electrostimulation was administered (Dantec CLAVIS, REF-9015A0012, Denmark). The stimulating current intensity was set at 10 Ma. EMS was stopped when the best contractility was observed and felt, and then 125 U of BTX was delivered into the each target muscle under US guidance. The same physiatrist (E.A.) who was blinded to the assessments scores conducted all the scans and injections. All patients performed post-treatment stretching exercises 60 min d⁻¹ for 2 weeks. In addition, each patient used an inhibitory wrist splint 6 h d⁻¹ for 2 months. Patients were instructed not to use oral anti-spastic medications for 3 months after the treatment.

Clinical and Functional Assessment

Spasticity was evaluated using the MAS (7) and Tardieu Scale (TRS) (8), and functional ability was assessed using the Barthel Index (BI) and Fugl-Meyer Motor Assessment Scale (FMS) at baseline, and at 2 weeks and 2 months post treatment. All patients were examined by the same physiatrist (U.D.), who was blinded to the treatment.

Statistical Analysis

Statistical analysis was performed using SPSS v.22.0 for Windows (IBM, Corp., Armonk, NY). The Kolmogorov Smirnov test was used to analyze normal distribution of variables. Friedman's test was used for multiple intergroup comparisons and the Wilcoxon signed-rank test were used for single intergroup comparisons. The level of statistical significance was set at $P < 0.05$.

Results

The study included 22 patients with upper limb spasticity that were recruited from among 43 stroke patients that presented to our outpatient clinic (Figure 1). The mean age of patients who treated with BTX (eight women and fourteen men) was 60.5 ± 11 years. All of the 22 patients completed the study and none of them declared adverse events or complications of injections. Patient demographics are shown in Table 1.

A significant reduction in the degree of spasticity (based on MAS and TRS) was observed at 2 weeks post treatment and persisted at 2 months post treatment ($P < 0.05$) (Table 2). Additionally, functional scores (based on BI and FMS) at 2 weeks and 2 months post treatment were significantly better than at baseline ($P < 0.05$) (Table 2).

Table 1. Patient characteristics

Age (yrs) (Mean ± SD)	60,5 ± 11
Sex (male / female)	14/8
Type of stroke (ischemic / hemorrhagic)	14/8
Duration of stroke (month) (mean ± sd)	44,3±68,9
Hemiplegic side (right / left)	13/9
SD: standard deviation, yrs: years	

Table 2. Clinical and functional assessments

Parameters	Before Tx	After Tx (at 2 weeks)	After Tx (at 2 mos)	<i>p</i> [*]	<i>p</i> [#]	<i>p</i> [†]
MAS						
<i>Biceps</i>	2,45 ±0,50	0,81 ±0,54	1,18 ±0,52	0,01	0,01	0,01
<i>Pronator</i>	2,72 ±0,45	0,68 ±0,47	1,11 ±0,34	0,01	0,01	0,01
<i>Wrist</i>	2,77 ±0,42	0,70 ±0,57	1,18 ±0,39	0,01	0,01	0,01
<i>Finger flexors</i>	2,72 ±0,45	1,00 ±0,46	1,25 ±0,42	0,01	0,01	0,01
Tardieu degree						
<i>Wrist</i>	2,54±0,59	0,90 ±0,75	1,22 ±0,68	0,01	0,01	0,01
Tardieu angle						
<i>Wrist</i>	52,04±6,29	15,22 ±6,45	22,27 ±6,67	0,01	0,01	0,01
Barthel Index	52,50±12,32	58,63 ±13,01	58,86 ±12,33	0,01	0,01	0,01
Fugl-Mayer Assessment	8,54±9,26	16,95 ±11,61	15,22 ±10,71	0,01	0,01	0,01

*Triple comparison of BT, 2 weeks AT and 2 months AT; #BT vs. 2 weeks AT; †BT vs. 2 months AT; *p* values in boldface are statistically significant

Discussion

The present findings show that significant improvement in spasticity and functional recovery was achieved using dual-guided BTX injection (US and EMS) for the treatment of upper extremity spasticity in chronic hemiplegic stroke patients. BTX injection in patients with stroke is performed via several methods, MNP, EMG, EMS, and US. The most important factor associated with the success of BTX injection is accurate needle placement into the targeted muscle (6). MNP is widely used for superficial and major muscles, and requires a good anatomical knowledge. A study in which the accuracy of MNP was monitored via US reported accuracy of 92.6% for m. gastrocnemius medialis and 64.7% for m. gastrocnemius lateralis (9). Another study monitored the accuracy of MNP via EMS, and reported accuracy of 13% for m. flexor carpi radialis and 16% for m. flexor carpi ulnaris (10). It can be considered that the achievement drive and reliability of MNP method is low, particularly for injections into small and deep-seated muscles such as forearm muscles, even when performed by experienced physicians (11).

It was reported that BTX injection performed close to the motor endplates might be most effective and EMG and EMS are reliable for muscle and motor endplate localization (12).

When performing BTX injection under EMG guidance it is easy to know when the needle is in a spastic muscle, but it is difficult to know if the needle is in the targeted muscle (13). Loss of selective muscle activation and over-activity of neighboring muscles negatively affects the accuracy of EMG. Additionally, needle EMG is associated with pain, which limits its use. Even though significant improvement was reported in patients with cervical dystonia following EMG-guided BTX injection (14), the technique may not be sufficient when used alone.

EMS is widely considered a reliable technique for the localization of a targeted muscle and motor endplate, although it is associated with the following disadvantages: it is a blind method, time is lost while guiding the needle into the targeted muscle, and it causes pain (11). In contrast, US is a more reliable, time-efficient, and painless method for muscle localization. It provides real-time imaging during injections and it can help physicians avoid accidental injection into neurovascular structures (15). Although it was reported that US-guided BTX injection is an alternative for BTX injection via EMG or EMS guidance, US is not reliable for motor endplate localization.

Several studies compared BTX injection methods, including MNP, EMG, EMS, and US, and US and EMS were reported to be superior to the other methods (4, 5, 9, 10, 16). Kwon et al. compared US and EMS guidance and reported a significant decrease in MAS and TRS scores in both groups of children with cerebral palsy at 1 month post injection; however, they also reported that the significant decreases in MAS and TRS scores persisted at 3 months post injection only in the US group (16). In the present study a significant reduction in the degree of spasticity

(based on MAS and TRS) was observed at 2 weeks post treatment and persisted at 2 months post treatment.

Picelli et al. reported that EMS and US guidance provided better results for all parameters (based on MAS, TRS and fingers passive range of motion) in stroke patients with wrist and finger flexor spasticity than MNP. In addition, they reported there weren't any significant differences between the EMS and US groups (4).

In an earlier study by Picelli et al. the accuracy of MNP-guided and EMS-guided BTX injection was monitored via US to determine if the needle was inserted into the correct muscle (5). They reported the accuracy of each method as follows: proximal part of m. gastrocnemius medialis: 88.09% in the MNP group versus 92.30% in the EMS group; distal part of m. gastrocnemius medialis: 92.86% in the MNP group, versus 94.87% in the EMS group; proximal part of m. gastrocnemius lateralis: 64.28% in the MNP group, versus 87.17% in the EMS group; distal part of m. gastrocnemius lateralis: 73.80% in the MNP group, versus 92.30% in the EMS group. These findings indicate that BTX injection via MNP is much less accurate than via EMS for muscles smaller than m. gastrocnemius lateralis, and in particular for forearm muscles. Despite observing that EMS was more accurate than MNP, they also reported that EMS is a blind method, as is MNP, and may cause neurovascular damage if it is the only method used (5).

It was reported that BTX injection into the upper extremity muscles in stroke patients can improve functional disability. Shaw et al. compared BTX injection and physiotherapy, in terms of functional improvement, and reported that 25.1% of the BTX group and 19.5% of the control group exhibited functional improvement (17). Although better results were achieved in BTX group at 1, 3, and 12 months post treatment, there wasn't a significant difference between the groups (17). In the present study BI and FMS scores at 2 weeks and 2 months post treatment were significantly better than at baseline. We think the significant improvement in functional scores observed in the present study was due to dual US and EMS guidance of BTX injections, and misapplications can be prevented with dual-guidance, particularly for injections into forearm muscles. In addition to improvement in spasticity and functional recovery, the dual-guided injection method minimized the occurrence of complications.

The present study has some limitation foremost the lack of a control group. The study's small sample size is another limitation, as is the short (2 months) follow-up period.

Conclusion

In conclusion, significant improvement in spasticity and functional recovery were achieved via dual-guided (US and EMS) BTX injections; this method might also be used to reduce the risk of neurovascular complications. Based on the present findings, we think US and EMS-guided BTX injections should be used in eligible patients for the treatment of spasticity and that larger-scale randomized clinical trials with longer follow-up periods are needed to

further delineate the effectiveness of the dual-guided BTX injection method described herein.

Conclusion

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Author's Contributions: Research concept and design (UD, EA); botulinum toxin injections (EA); data collecting (UD), All authors approved the final version of the manuscript

Ethical issues: All Authors declare, Originality and ethical approval of research. Responsibilities of research, responsibilities against local ethics commission are under the Authors responsibilities. The study was conducted under defined rules by the Local Ethics Commission guidelines and audits.

References

1. Monaghan K, Horgan F, Blake C, et al: Physical treatment interventions for managing spasticity after stroke (Protocol), 2011 The Cochrane Collaboration, Published by John Wiley & Sons Ltd., The Cochrane Library 2011, Issue 7.
2. Ozcakir S, Sivrioğlu K. Botulinum toxin in poststroke spasticity. *Clinical medicine and Research* 2007;5(2):132-8.
3. Çeliker R. Bölüm 58, Spastisite Tedavisinde Kullanılan İlaçlar, Fiziksel Tıp ve Rehabilitasyon, 2. Baskı, (Ed: Beyazova M, Kutsal YG), 2011;2:901-17.
4. Picelli A, Lobba D, Midiri A, et al: Botulinum toxin injection into the forearm muscles for wrist and fingers spastic overactivity in adults with chronic stroke: a randomized controlled trial comparing three injection techniques, *Clin Rehabil* 2014; 28(3): 232-42.
5. Picelli A, Bonetti P, Fontana C, et al: Accuracy of botulinum toxin type A injection into the gastrocnemius muscle of adults with spastic equinus: manual needle placement and electrical stimulation guidance compared using ultrasonography. *J Rehabil Med* 2012; 44(5): 450-2.
6. Wissel J, Ward AB, Erztgaard P, et al. European consensus table on the use of botulinum toxin type A in adult spasticity. *J Rehabil Med* 2009; 41:13-25.
7. Bohannon RW, Smith MB: Interrater reliability of a modified Ashworth scale of muscle spasticity. *Phys Ther* 1987;67:206-7
8. Paulis WD, Horemans HL, Brouwer BS, Stam HJ. Excellent test-retest and interrater reliability for Tardieu Scale measurements with inertial sensors in elbow flexors of stroke patients. *Gait Posture* 2011; 33(2): 185-9
9. Yang EJ, Rha DW, Yoo JK, et al. Accuracy of manual needle placement for gastrocnemius muscle in children with cerebral palsy checked against ultrasonography. *Arch Phys Med Rehabil* 2009; 90:741-4.
10. Chin TY, Natrass GR, Selber P, et al. Accuracy of intramuscular injection of botulinum toxin A in juvenile cerebral palsy: a comparison between manual needle placement and placement guided by electrical stimulation. *J Pediatr Orthop* 2005; 25:286-91.
11. Schroeder AS, Berweck S, Lee SH, Heinen F. Botulinum toxin treatment of children with cerebral palsy- a short review of different injection techniques. *Neurotoxicity Research* 2006; 9:189-96.
12. Shaari CM, Sanders I. Quantifying how location and dose of botulinum toxin injections affect muscle paralysis. *Muscle Nerve* 1993;16 (9):964-9.
13. G. Sheean, N. A. Lanninb, L. Turner-Stokes, et al. Botulinum toxin assessment, intervention and after-care for upper limb hypertonicity in adults: international consensus statement, *European Journal of Neurology* 2010;17:74–9.
14. Comella CL, Buchman AS, Tanner CM, et al. Botulinum toxin injection for spasmodic torticollis: increased magnitude of benefit with electromyographic assistance. *Neurology* 1992;42(4):878-82
15. Henzel MK, Munin MC, Niyonkuru C, et al. Comparison of surface and ultrasound localization to identify forearm flexor muscles for botulinum toxin injections. *PM & R: the journal of injury, function, and rehabilitation* 2010;2:642-6.
16. Kwon JY, Hwang JH, Kim JS. Botulinum toxin a injection into calf muscles for treatment of spastic equinus in cerebral palsy: a controlled trial comparing sonography and electric stimulation-guided injection techniques: a preliminary report. *Am J Phys Med Rehabil* 2010; 89:279-86.
17. Shaw LC, Price CI, van Wijck FM, et al. Botulinum Toxin for the Upper Limb after Stroke (BoTULS) Trial: effect on impairment, activity limitation, and pain. *Stroke* 2011;42:1371-9.

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