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OPEN ACCESS JOURNAL ISSN: 2148-6832

MSD Medical Science and Discovery
2018; 5(9):326-30

Research Article Doi: 10.17546/msd.460182

An effective approach for botulinum toxin injection in patients with stroke for focal spasticity: dual guidance

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Abstract

Objective: There are several studies in the literature focusing the guided botulinum toxin injections into the spastic muscle. However, these guides were applied separately and their effectiveness was compared among themselves. We could not find any study investigating the effectiveness of combined 2 guides in the literature. This study aimed to compare the efficacy of botulinum toxin injections, applied to the upper limb muscles of the stroke patients in our clinic who have being diagnosed with focal spasticity, that are performed via ultrasonography and ultrasonography + electrical muscle stimulator guidance.

Materials and Methods: Electronic data on 62 hemiplegic stroke patients with grade 2 and 3 focal spasticity who had received botulinum toxin injections into their upper limb muscles by the same physician, who used similar protocol and recorded the results, were scanned retrospectively. The spasticity of the patients in both groups was assessed with the Modified Ashworth Scale at the end of two weeks and three months.

Results: A statistically significant difference was found between the Modified Ashworth Scale values of both groups in terms of all muscles, compared to the values seen in the pre-treatment period ($p<0.05$). The Modified Ashworth Scale values at 3 months posttreatment in ultrasonography + electrical muscle stimulator group were not statistically different from those at 2 weeks posttreatment, with respect to wrist flexion and finger flexion. In intergroup comparison, there was no statistically significant difference between the Modified Ashworth Scale values at pretreatment and 2 weeks posttreatment. However, statistically significant difference in all muscle groups was found in favor of the ultrasonography + electrical muscle stimulator group at 3 months posttreatment controls ($p<0.05$).

Conclusion: Upper limb spasticity due to stroke can be substantially recovered with botulinum toxin injections that are applied via only ultrasonography guidance or via ultrasonography + electrical muscle stimulator guidance. According to data from the assessment at 3 months posttreatment, the botulinum toxin injection performed via ultrasonography + electrical muscle stimulator guidance had more positive effects.

Key words: stroke, muscle spasticity, botulinum toxin, injections, electrical muscle stimulation

Introduction

Stroke is a medical condition that most leads to disability and dependency (1). Spasticity is known to be among the complications most frequently seen following a stroke. Upper limb spasticity, a common complication after stroke, results in a decrease in the quality of life by impairing the functions of the limbs (2; 3). In spasticity treatment, non-invasive methods should be applied first before turning to invasive methods (4). In cases where the spasticity affects a specific muscle group, local treatments should be preferred. The most common local treatment for focal spasticity is botulinum toxin (BTX) injection. (5). In clinical practice, intramuscular BTX injection can be applied using several types of guidance, including manual needle placement (MNP), electromyography (EMG), electrical muscle stimulation (EMS), and ultrasonography (USG). Today, many clinics frequently perform BTX applications together with the MNP technique, considering that the anatomic points of muscles are known very well (6). On the other hand, BTX applications under the guidance have several advantages, such as being able to identify the proper localization of the muscle and the target point in the muscle and not causing harm to surrounding structures (7). This study aimed to compare the efficacy of BTX injections, applied to the upper limb muscles of the patients in our clinic who have being diagnosed with focal spasticity, that are performed via USG and USG+EMS guidance by scanning the data of the patients retrospectively.

Received 15-09-2018 **Accepted** 20-09-2018 **Available Online** 30-09-2018
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http://dx.doi.org/10.17546/msd.460182

Material and Methods

In this study, electronic data on 62 hemiplegic stroke patients with grade 2 and 3 focal spasticity who presented to our clinic between May 01, 2013 and May 01, 2018 and had received BTX injections into their upper limb muscles by the same physician, who used similar protocol and recorded the results, were scanned retrospectively. As this was a retrospective study, approval from an ethics committee was not required.

Inclusion Criteria

1. Male and female patients, between the ages of 18 and 80 with stroke-driven focal spasticity, who were administered BTX injection to m. biceps brachii (BB), pronator teres (PT), m. flexor carpi radialis (FCR), m. flexor carpi ulnaris (FCU), m. flexor digitorum superficialis (FDS) and m. flexor digitorum profundus (FDP) muscles, via USG guidance.
2. Male and female patients, between the ages of 18 and 80 with stroke-driven focal spasticity, who were administered BTX injection to BB, PT, FCR, FCU, FDS and FDP muscles, via USG+EMS guidance.
3. The patients who had level 2 or level 3 spasticity according to the Modified Ashworth Scale (MAS) before the treatment.

Exclusion Criteria

1. Male and female patients, between the ages of 18 and 80 with stroke-driven focal spasticity, who were administered BTX injection to BB, PT, FCR, FCU, FDS and FDP muscles, applied by MNP technique.
2. The patients who were unable to come to the two-week and/or three-month control check-up following BTX, or whose examination records on these dates could not be found.
3. The patients who had level 1 and level +1 spasticity in the specified muscles according to the MAS before the treatment.

Protocol

BTX injections were administered by the same physician to the patients of both groups under sterile conditions as they were in supine position. During the applications, all of the patients were administered Botulinum Toxin Type A (Dysport) diluted with saline solution, which contained 2.5 ml of 0.9 percent sodium chloride. The patients for whom only USG, and USG+EMS were applied as the guide procedure over the course of BTX administration are defined as USG group, and USG+EMS group, respectively.

The spasticity of the patients in both groups was assessed with the MAS at 2 weeks and 3 months posttreatment.

Statistical analysis

Statistical analyses were performed using commercially available statistical software (SPSS, version 22.0; SPSS, Inc., Chicago, IL). The Kolmogorov Smirnov test was applied to determine whether the data were in accord with normal distribution or not, the results of which showed that the data did not have normal distribution. The chi-square test and Mann-Whitney U test were used for discrete data and continuous data to determine whether there were any statistically significant differences between the demographic data and the initial assessments (MAS), respectively. The existence/absence of any statistically significant differences between assessments at baseline, and at 2 weeks and 3 months post treatment within the group was determined by applying the Friedman test. Statistical significance was accepted at $p<0.05$. After the determination of a statistically significant difference, post-hoc (paired comparisons) analysis was performed using the Wilcoxon test. Bonferroni correction was also applied, and $p<0.005$ was taken as the significance coefficient. Mann-Whitney U test was applied to see whether there was any statistical intergroup difference between assessments at baseline, and at 2 weeks and 3 months posttreatment.

Results

The demographic data of the patients included in the present study are given in Table 1. Although the groups were homogeneous with respect to age, gender, duration of disease, hemiplegic side, the presence of hypertension, and the presence of hyperlipidemia, homogeneity was not observed in terms of the presence of diabetes mellitus and history of smoking. No statistically significant difference was detected between the MAS values of the groups before the treatment ($p>0.05$).

A statistically significant difference was found between the MAS values of both the USG group and the USG+EMS group in terms of all muscle groups, compared to the values seen at baseline.($p<0.05$).

Results from the intragroup paired comparison according to MAS parameters in the USG group showed that the decrease in MAS values measured at 2 weeks and at 3 months posttreatment was statistically significant compared to baseline ($p<0.005$). Moreover, there was a statistically significant difference between the MAS values at 2 weeks and 3 months posttreatment; that is, there was an increase in MAS values (Table 2).

Results of the intragroup paired comparison of the change in the MAS parameters in the USG+EMS group showed that the decrease of the MAS values at 2 weeks and 3 months posttreatment were statistically significant compared to baseline($p<0.005$). The MAS values at 3 months posttreatment were not statistically different from the values at 2 weeks posttreatment, with respect to wrist flexion and finger flexion. However, the increase in the MAS values of elbow flexion and forearm pronation at 3 months posttreatment compared to 2 weeks posttreatment was found to be statistically significant (Table 3).

In intergroup comparison, there was no statistically significant difference between the MAS values at baseline and 2 weeks posttreatment. However, statistically significant difference in all muscle groups was found in favor of the USG+EMS at 3 months posttreatment ($p<0.05$) (Table 4).

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Table 1. Patients Demographic characteristics

Parameters	USG Group (n=22)	USG+EMS Group (n=22)	p
Age (yrs) (mean ± sd)	59,81±11,54	60,13±10,87	>0,05
Sex (male / female)	14/8	14/8	>0,05
Duration of stroke (month) (mean ± sd)	43,09±36,19	44,31±68,91	>0,05
Type of stroke (ischemic / hemorrhagic)	19/3	14/8	**<0,05**
Hemiplegic side (right / left)	12/10	15/7	>0,05
Diabetes Mellitus (+/-)	8/14	1/21	**<0,05**
Hypertension (+/-)	13/9	13/9	>0,05
Hyperlipidemia (+/-)	9/13	8/14	>0,05
History of smoking (+/-)	5/17	10/12	**<0,05**

sd: standard deviation, yrs: years

Table 2. Intragroup Comparisons of USG group. (PT: Post-Treatment)

Modified Ashworth Scale	Baseline	PT 2 weeks (median)(min/max)	PT 3 months	p
Elbow flexion	2 (2-3)	1 (1-2)	2 (1-3)	**<0,05**
Wrist flexion	3 (2-3)	1 (0-1+)	1+ (1-2)	**<0,05**
Hand flexion	3 (2-3)	1+ (1-1+)	1+ (1-2)	**<0,05**
Forearm pronation	3 (2-3)	1+ (0-1+)	1+ (1-2)	**<0,05**

Table 3. Intragroup Comparisons of USG+EMS group

Modified Ashworth Scale	Baseline	PT 2 weeks (median) (min/max)	PT 3 months	p
Elbow flexion	2 (2-3)	1 (0-1+)	1 (0-2)	**<0,05**
Wrist flexion	3 (2-3)	1 (0-1+)	1 (0-2)	**<0,05**
Hand flexion	3 (2-3)	1 (0-1+)	1 (0-2)	**<0,05**
Forearm pronation	3 (2-3)	1 (0-1)	1 (0-1+)	**<0,05**

Tablo 4. Intergroup Comparisons

Modified Ashworth Scale		USG median (min/max)	USG+EMS median (min/max)	p
Baseline	**Elbow flexion**	2 (2-3)	2 (2-3)	>0,05
	Wrist flexion	3 (2-3)	3	>0,05
	Hand flexion	3 (2-3)	3 (2-3)	>0,05
	Forearm pronation	3 (2-3)	3	>0,05
PT 2 weeks	**Elbow flexion**	1 (1-2)	1 (0-1+)	>0,05
	Wrist flexion	1 (0-1+)	1 (0-1+)	>0,05
	Hand flexion	1+ (1-1+)	1 (0-1+)	>0,05
	Forearm pronation	1+ (0-1+)	1 (0-1)	>0,05
PT 3 months	**Elbow flexion**	2 (1-3)	1 (0-2)	**<0,05**
	Wrist flexion	1+ (1-2)	1 (0-2)	**<0,05**
	Hand flexion	1+ (1-2)	1 (0-2)	**<0,05**
	Forearm pronation	1+ (1-2)	1 (0-1+)	**<0,05**

http://dx.doi.org/10.17546/msd.460182

Discussion

In the present study evaluating the efficacy of BTX injections on focal spasticity, applied to upper limb muscles combined with USG or USG+EMS, statistically significant decrease in spasticity was observed in both groups compared to baseline. BTX injection applied via USG+EMS guidance was found to be a superior treatment method for reducing spasticity in the long term.

BTX injection is an effective, safe and local treatment method for stroke patients with focal or multifocal spasticity. BTX injection can be performed either through the MNP technique without using any guide, or together with guides, such as EMS, USG, and EMG (7; 8; 9; 10).

Although the MNP technique is commonly used on superficial and large muscles, it requires good knowledge of anatomy. When performing BTX injection under EMG guidance it can be ensured that the needle is in a spastic muscle, but it is difficult to know if the injection is applied to the targeted muscle (11). Various studies which controlled the accuracy of the MNP technique reported that the accuracy rates for the gastrocnemius medialis muscle, gastrocnemius lateralis, hip adductors, medial hamstring, tibialis posterior, BB, PT, adductor pollicis, FCR and FCU were 92.6%, 64.7%, 67%, 46%, 11%, 62%, 35%, 22%, 13% and 16%, respectively (8; 10) Therefore BTX applications under the guidance of USG or EMS, for deeply located and small muscles, is recommended (7; 12; 13).

In the literature, there are numerous studies comparing BTX applications performed with different guides. Kwon et al. compared the efficacy of BTX injections applied via USG and EMS guidance on children with cerebral palsy who had equine deformity secondary to m. gastrocnemius spasticity. They observed a significant decrease in spasticity levels in both groups at 1 month posttreatment according to the MAS and Tardieu Scale (TS); however, they also reported that the significant decreases in spasticity persisted at 3 months posttreatment only in the USG group (9).

Picelli et al. compared the data obtained by applying BTX to the forearm muscles for the spasticity in stroke patients using three different injection techniques; MNP, EMS and USG (7). The patients were evaluated based on MAS, TS and the level of passive joint range of motion, with respect to the spasticity of the wrist and finger, at 4 weeks after the treatment. The EMS and USG groups had better results than the MNP group in terms of all parameters. No statistically significant difference was reported between the EMS and USG groups.

In another study by Picelli et al. which compared the accuracy of BTX applications under the guidance of MNP and EMS in stroke patients with equine deformity due to ankle plantar flexor spasticity, the accuracy of EMS method was found to be higher than MNP. However, they identified the EMS as a blind method just like the MNP method (12).

It was stated that BTX injection applied via USG guidance is superior than the other guide methods, with regard to protection of neurovascular structures, as well as application to the right muscle. However, BTX penetrates to the cell membrane with receptor mediated endocytosis and cannot enter the nerve cytosol by directly passing the cell membrane. Therefore, the effect of the toxin injection on a hyperactive muscle is directly related to the amount of toxins in the neuromuscular product. Thus, injections that target motor endplates are important for achieving optimum therapeutic effect with lower doses and less side effects. In this sense, the injection to be performed via EMS guidance is seen as the most appropriate method (14-15).

In the present study, we evaluated the effect of BTX injections under the guidance of USG or USG+EMS on spasticity according to only the MAS values at 2 weeks and 3 months posttreatment. The decrease in spasticity for both groups was statistically significant. It was further found that the decrease in the spasticity of wrist flexors and finger flexors that were observed in the USG+EMS group at 2 weeks posttreatment continued at 3 months posttreatment. Moreover, the data obtained from USG+EMS group at 3months posttreatment was found to be statistically better than USG group. We believe that this difference obtained not only is emerged as a result of the BTX injection to the correct muscle via USG guidance, but also as a result of the injection to the region with the densest motor endplates via EMS guidance.

Additionally, there were no complications in either group during the applications. Both methods are considered to be reliable.

Conclusion

There are several studies in the literature focusing the guided BTX injections into the spastic muscle. However, these guides were applied separately and their effectiveness was compared among themselves. We could not find any study investigating the effectiveness of combined 2 guides. In addition, one of the guiding methods (USG) we used in our study aims to find the right muscle for the injection while the other (EMS) aims to find the correct point in the right muscle.

In the present study, upper limb spasticity due to stroke can be substantially recovered with BTX injections that are applied via only USG guidance or via USG+EMS guidance. According to data from the assessment at 3 months posttreatment, the BTX injections performed via USG+EMS guidance had more positive effects. Randomized, controlled and prospective studies with larger patient groups would bring greater understanding to this subject.

Acknowledgement: None

Conflict of Interest: The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Author's Contributions: EA, MK: Research concept and design, Patient treatment applications, data collecting, analysis and interpretation of data. **EA:** Preparation of article and revisions. 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.

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