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Functional outcomes following ultrasound-guided botulinum toxin type A injections to reduce spastic equinovarus in adult post-stroke patients

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ABSTRACT

Objective: The aim of this study is to identify the effect on spasticity and walking of US-guided botulinum toxin type A (BoNT-A) injections administered to improve equinovarus walking pattern commonly observed in patients after stroke.
Material and method: Twenty-three patients with post-stroke spastic equinovarus deformity were recruited. The US-guided BoNT-A injections were administered into the spastic muscles (including gastrocnemius; GK, soleus; S and tibialis posterior; TP) using a specific approach, and all of the patients were enrolled in rehabilitation programmes after the injections. Modified Ashworth Scale (MAS), Brunnstrom stage of lower limb, Functional Ambulation Score (FAS), Preferred Gait Speed (PGS) and the six-minute walk test (6MWT) were assessed at the baseline, 4 and 12 weeks after the BoNT-A injection.
Results: Significant decreases in the MAS scores of the lower limb muscle (GK, S and TP) tone were measured 4 and 12 weeks after the BoNT-A injection when compared to the baseline scores ($p < 0.05$). In parallel with a reduction in spasticity there was an increase in 6MWT and PGS in the 4th and 12th weeks. Increases in motor improvement and functional ambulation score were ensured in the 12th week ($p < 0.05$).
Conclusion: Spastic equinovarus deformity observed in patients after stroke creates significant limitations in the patient's functional walking speed and distance. As a result, when BoNT-A injections accompanied by ultrasound to improve equinovarus deformity considering the innervation zones of the muscles with a specific approach are administered directly into the muscle at the correct point, we can say it provides hopeful results from a functional point of view.

1. Introduction

Stroke is a commonly encountered neurological problem that may cause death and disability (Özcan, 1995). One of the clearest aims in treatment of stroke patients is to get the patient walking again. Ensuring walking again with a regular walking pattern is among the most common and primary reasons for attending rehabilitation clinics (Dalyan and Çakci et al., 2004).

Spasticity develops in 20–40% of stroke patients (Erhan, 2016). The muscles in the lower extremities with most common spasticity after stroke are the knee extensors, ankle plantar flexors and foot invertors. In hemiplegic patients visual walking analysis identifies slow, spastic walking with weak coordination and asymmetry in these patients. The patient has long swing phase and short stepping phase on the affected side. The contact between foot and ground is on the front part and lateral edge of the foot. Situations causing this pattern are spasticity of ankle plantar flexors during foot inversion along with weakness of the foot dorsiflexors and foot evertors (Dalyan and Çakci et al., 2004). As a result patients walk unsafely and at low speed. Spastic equinovarus foot (SEVF) is one of the most common disabling deformities observed among hemiplegic patients. SEVF is frequently associated with other kinematic gait abnormalities, such as stiff knee gait, genu recurvatum, and painful claw toes. SEVF deformity forces the patient to increase their hip and knee flexion in the swing phase. If they are unable to do this (e.g., if they have associated stiff knee gait), the patient will present a hip circumduction in the swing phase. Correction of such equinus may therefore improve distal as well as proximal gait disturbances

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Walking rehabilitation in hemiplegic patients corrects the asymmetry present in walking and organises treatment programs to weaken spastic muscles and strengthen weak muscles to ensure the patient develops safe and independent normal walking (Mauritz, 2004).

Botulinum toxin type A (BoNT-A) inhibits acetylcholine release from the nerve endings, creating a presynaptic neuromuscular block, and is used for the local treatment of spasticity. To identify the target muscle for BoNT-A administration, a variety of guides can be used, like anatomical palpation, electromyography, muscle stimulation and ultrasound (US), and there are a variety of applications used for the injection methods. US is a well-established, reliable and reproducible imaging method for defining muscle anatomy, and a US system with a 7.5 MHz linear transducer can provide sufficient resolution for both superficial and deep-seated muscles (Willenborg, 2002). An injection method identifying the target muscle and applied to the innervation zone of the muscle via US guidance is very effective (Kaymak, 2017a).

In this study we aimed to identify the effect on spasticity and walking of US-guided BoNT-A injections accompanied by a specific guide prepared according to innervation zones to improve the equinovarus walking pattern commonly observed in stroke patients.

2. Materials and methods

2.1. Patients

Patients applying to our clinic from March to October 2017 after ischemic or haemorrhagic strokes were assessed, and those with at least stage 1 spasticity of the ankle according to the Modified Ashworth Scale (MAS) were included in this study. The exclusion criteria were the presence of MAS stage 4 spasticity, less than 3 months or more than 12 months since the stroke, the presence of fractures or contractures of the lower extremities, receiving any other medical treatment for spasticity, a botulinum toxin allergy or an infection in the injection area, breastfeeding and pregnancy. The Malatya Clinical Research Ethics committee granted permission for this study, and the patients or patients' relatives provided written consent for the application.

3. Treatments

3.1. US-guided BoNT-A injections

We applied BoNT-A to the following muscles: gastrocnemius (GC), soleus (S) and tibialis posterior (TP). Each of the patients underwent US-guided BoNT-A injections, with B-mode real-time US using an Esaote MyLab 70 with a linear transducer (scanning frequency 6–18 MHz) to guide the needle positioning into the targeted muscle at each injection site. The injection was performed by a physiatrist according to the EURO-MUSCULUS/Ultrasound Study Group in Physical and Rehabilitation Medicine (USPRM) spasticity approach (Kaymak, 2017a). The BoNT-A was injected at 2 sites with 25 U each for the GC medial head, GC lateral head, S, and TP.

All of the patients received one set of BoNT-A injections in their spastic muscles. To avoid differences in the dose calculations, all of the patients received BoNT-A (OnabotulinumtoxinA, BOTOX®; Allergan, Turkey) diluted with 2 mL of 0.9% saline administered with a 25 gauge needle.

3.2. Rehabilitation program

Spastic equinovarus foot rehabilitation programmes (including strengthening of the tibialis anterior and peroneus muscles, electrical stimulation, stretching of the triceps surae) was initiated 1 day after the BoNT-A injection to reduce spasticity and prevent contracture, and gait and balance training. The exercise program continued for 10 weeks, with three sessions per week and 50 min for each session; then, home training was performed for three sessions each week, 50 min each session, for 2 weeks. The family members were trained by a therapist to complete the home training with the patients. Re-assessments of the Brunnstrom stage, Modified Ashworth Scale (MAS), Functional ambulation score (FAS), gait distance and speed were performed 4 and 12 weeks after the BoNT-A injection.

4. Assessments

4.1. Evaluation of motor recovery (Brunnstrom stage)

The Brunnstrom staging system, which is a motor and tonus analysis system, was used to specify six possible grades for the upper extremity, hand and lower extremity. The flask period without even the lowest level of desired motion is stage 1, while the presence of isolated movements is assessed as stage 6 (Sawner and Lavigne, 1992).

4.2. Modified Ashworth Scale (MAS)

MAS measures resistance during passive soft-tissue stretching. It is a quick and easy measure that can help assess the efficacy of treatment. The MAS scores were recorded to evaluate the degree of spasticity. The evaluation standards refer to a grading system score on a scale of 0–4, where 0 shows normal muscle tone, 1 is a slight increase in muscle tone at the end of the range of motion, 1+ is a slight increase in muscle tone through less than half of the range of motion, 2 is a more marked increase in muscle tone through most of the range of motion, 3 is a considerable increase in muscle tone, and 4 is a rigid joint. For statistical purposes, a score of 1 was considered to be 1, 1 + was 2 and scores of 2, 3 and 4 were 3, 4 and 5, respectively (Bohannon and Smith, 1987).

Functional Ambulation Score (FAS): Classifies functional ambulation of a patient with difficulty walking under 6 headings. A patient with a score of 0 cannot walk at all, while a patient with 5 points can independently ambulate (Collen, 1990).

Preferred Gait Speed (PGS): The participants were instructed to walk for 10 m at their self-selected speed. The time to complete the task was recorded and the distance was divided by time to obtain gait speed (m/s) (Peters, 2013).

6 Minutes Walking Test (6MWT): Patients were requested to walk at their own chosen speed. When required support or assisting devices are allowed. Patients walk a fixed distance of 20 m back and forth until the end of the duration and the distance is recorded (Fulk, 2008).

4.3. Statistical analysis

We conducted descriptive analyses to summarize the patients' baseline characteristics (age, gender and time from stroke onset), and all of the data measured are represented as mean ± standard deviation. The pretreatment and follow-up clinical evaluation scores were analysed using the nonparametric Wilcoxon matched-pairs signed-rank test without assumptions about the normality of the data. The Bonferroni correction was used for multiple comparisons. IBM SPSS Statistics ver. 18.0 was used for all of the

Table 1
Demographic and clinical features of the patients.

Age, years (SD)	58.8 ± 9.8
Duration of disease, months (SD)	8.4 ± 3.1
Male/Female, n(%)	12(53)/11(47)
Type of stroke, n(%)	
Cerebral infarction	19(83)
Cerebral haemorrhage	4(17)
Side of hemiparesis, right/left n(%)	14(60)/9(40)

SD: standard deviation.

analyses, and a p-value <0.05 indicated statistical significance for all of the tests.

5. Results

Twenty-three post-stroke patients (12 females and 11 males) were recruited for this study, and their mean age was 58.8 ± 9.8 years old (range 35–70 years). The mean duration from disease onset was 8.4 ± 3.1 months (range 3–12 months). Nineteen patients had cerebral infarctions and only four had cerebral haemorrhages. In addition, 14 patients had right hemiplegia and 9 had left hemiplegia. No apparent adverse effects were observed during the follow-up times, and all of the patients completed the initial, 4-week and 12-week assessments after the injection (Table 1). No side effects were observed in any of our patients.

5.1. MAS assessment

All of the patients showed improvements in their muscle tone according to the MAS scores 4 and 12 weeks after the treatment session ($p < 0.05$) (Table 2).

5.2. Motor recovery (Brunnstrom stage) assessment

The Brunnstrom stage for lower extremity advanced from stage 3 to stage 4 at 12 weeks after the injection (Table 2).

5.3. FAS assessment

In parallel with the Brunnstrom stage, evaluations of the functional ambulation scale of patients 12 weeks after injections found that one person had advanced from dependent walking (FAS = 2) to observer dependent walking level (FAS = 3) (Table 2).

Gait speed and distance outcomes: The 10 m walking speed continuously increased in the 4th and 12th weeks (0.16 ± 0.06 m/s; 0.17 ± 0.06 m/s; 0.19 ± 0.06 m/s, respectively). Similarly the 6 min walking test measurements continuously increased in the 4th and 12th weeks (54.7 ± 22.2 m, 58.2 ± 21.8 m, 64.5 ± 22.5 m, respectively). Both speed and distance increases were statistically significant in the 4th and 12th weeks after injection ($p < 0.05$).

6. Discussion

In this study, the US-guided BoNT-A injections according to the innervation zones of the muscles reduced the lower limb spasticity and improved equinovarus in functional outcomes especially for gait in post-stroke patients.

In hemiplegic patients equinus deformity of the foot is commonly accompanied by varus deformity. Improper limb clearance and lack of appropriate foot posture result in a tendency to totter/fall. Hitchhiker's big toe/clawing toes lead to difficulties while using ankle/foot orthosis and wearing shoes. In both spastic hemiplegic children and in the presence of lower extremity spasticity after stroke, the ankle primary invertor muscle of the tibialis posterior muscle should definitely be assessed. Botulinum toxin injections for the gastrocnemius and soleus in the lower extremity generally are seen as easy by clinicians due to being both surface and large muscles; however in recent years many studies have concluded that botulinum toxin type A injections for equinus deformity are more effective when accompanied by ultrasound (Picelli, 2012). Although needle insertion into the tibialis posterior for botulinum toxin injection is usually performed using anatomic landmarks for guidance, the tibialis posterior is considered to be one of the least accessible muscles for needle placement because it is located deep within the lower leg (Rha, 2010; Wissel, 2009). In addition, neurovascular bundles of the lower leg may be unintentionally injured during the procedure because they adjoin the tibialis posterior closely and variously. The authors previously reported that ultrasonographic guidance might be more helpful for needle placement to the tibialis posterior in adults because it increases accuracy and reduces neurovascular injury rates when compared with conventional needle insertion under anatomic landmark guidance. Tibialis posterior muscle can easily be demonstrated under the tibialis anterior muscle and the interosseous membrane. Therefore tibialis posterior injections should be performed cautiously with anterior approach under US-guided in order to avoid injury to the nerve or artery (Rha, 2010).

The chemo denervation effect of BoNT-A on muscle tissue is linked to the toxin reaching the presynaptic membranes (neuromuscular junctions). The area within the muscle where the neuromuscular junctions are located is called the end-plate region, and those areas with dense end-plate regions are called innervation zones. For the BoNT-A injections to be more effective, it is important that the toxin reach the innervation zone; however, the innervation zones do not display clear differences depending on the person (Kaymak, 2017b). We believe that US-guided BoNT-A injections into the innervation zones using the Euro-musculus approach for the lower extremity muscles allows one to administer more appropriate injections, even for deep muscles. The reduced spasticity obtained, functional gains for the lower extremities and continuation, even in the 12th week, allow us to make this interpretation. Additionally, as a standard approach for

Table 2
Changes in the Brunnstrom stage, MAS and FAS scores measured before the BoNT-A injection and 4 and 12 weeks after (mean ± standard deviation).

Items	Pretreatment (n:25)	4 weeks after injection (n:25)	P_1 value	12 weeks after injection (n:25)	P_2 value
FAS Median(IQR)[a]	2(1)	2(1)		3(1)	
MAS Ankle-food	2.69 ± 0.55	2.08 ± 0.41	(p < 0.05)	1.69 ± 0.47	(p < 0.05)
Brunnstrom stage	3(1)	3(1)		4(1)	
Lower limb					
Median (IQR)[a]					
6 mt walking test (mt)	54.7 ± 22.2	58.2 ± 21.8	(p < 0.05)	64.5 ± 22.5	(p < 0.05)
20 mt Walking test (mt/sn)	0,16 ± 0,06	0,17 ± 0,06	(p < 0.05)	0,19 ± 0,06	(p < 0.05)

[a] Median interquartile range, MAS: Modified Ashworth Scale, FAS: Functional ambulation scale, BoNT-A: botulinum toxin type A. All p values were adjusted with the Bonferroni correction. Statistically significant difference ($p < 0.05$) when compared to the value before the injection.

clinicians administering injections, the use of this approach is effective for practical and applied results.

Reducing spasticity along with gaining motor function after botulinum toxin injection is the main aim of rehabilitation treatment after stroke. In the literature there is debate about the topic of the correlation between spasticity and function. Wissel et al. (2010) found that stroke patients with spasticity had lower Barthel index points and quality of life scores when compared with non-spastic patients. BTX-A injections do not treat contracture or improve functions of hemiparetic extremities alone; however they create a "window of opportunity" for functional improvement as part of a focused treatment programme by reducing abnormal sensory inputs and uncontrolled alpha motor activity (Ward, 2008). As a result the importance of rehabilitation programmes after botulinum toxin injections is emphasised in many studies. In our study the continuation of functional gains and effects up to 3 months later of patients included in a variety of physical therapy and rehabilitation programmes supports this information.

Lamontagne et al. (2001) reported that plantar flexor spasticity is a factor contributing to walking performance, especially walking speed. Sommerfeld et al. (2004) measured the Rivermead Mobility Index and Get Up and Go test and reported the functional scores of patients without spasticity were significantly better. Non-spastic patients showed better performance on the Barthel Index measuring daily life activities compared to spastic patients. A recent publication observed an increase in walking speed and distance in two of 3 patients 10 weeks after botulinum toxin injection in patients with post-stroke equinovarus deformity (Priya, 2017). Fock et al. (2004) evaluated patients with equinus deformity after traumatic brain injury in the 3rd month after botulinum toxin injections and observed that there was an increase in walking speed together with a reduction in spasticity. In our study, we used data as recommended by the Mont-Godinne group (Deltombe, 2017). However, we did not use video walking analysis to assess kinetic and kinematic walking parameters. In parallel with the reduction in ankle spasticity in our patients, we identified significant improvements in waking speed and walking distance compared to values before treatment. However, mean walking speeds were very low. In this groups with high rates of aided walking even at low walking speeds, we only encountered observer-based functional gain, one of the aims of treatment. In long term follow-up of these patients with only a single dose injection administered and still attending rehabilitation programs, we aim to see better functional results.

7. Conclusion

Botulinum toxin type A injections accompanied by ultrasound are effective when used for local treatment of spasticity commonly observed post-stroke in lower extremities and for treatment of spastic equinovarus deformity affecting patient walking. We wish to emphasise that the administration method using the specific approach (Euromus approach) is effective, reliable and easily applied in practice.

7.1. Limitations

The lack of objective video-supported walking analysis of stroke patients with equinovarus deformity is the most significant limitation of our study.

Transparency document

Transparency document related to this article can be found online at https://doi.org/10.1016/j.toxicon.2018.03.003.

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