SHORT COMMUNICATION

ACCURACY OF BOTULINUM TOXIN TYPE A INJECTION INTO THE FOREARM MUSCLES OF CHRONIC STROKE PATIENTS WITH SPASTIC FLEXED WRIST AND CLENCHED FIST: MANUAL NEEDLE PLACEMENT EVALUATED USING ULTRASONOGRAPHY

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Objective: To investigate the accuracy of manual needle placement for injection of botulinum toxin type A into the forearm muscles of adults with spastic flexed wrist and clenched fist as a consequence of stroke.

Design: Prospective clinical study.

Patients: A total of 41 adults with chronic stroke who were scheduled to receive botulinum toxin type A injection into the following forearm muscles: flexor carpi radialis, flexor carpi ulnaris, flexor digitorum superficialis and flexor digitorum profundus.

Methods: According to Huber & Heck’s atlas suggestions on treatment of spasticity with botulinum toxin, surface identification of muscles to inject was performed by means of palpation and anatomical landmarks. Accuracy of needle placement and muscle thickness at the site of needle insertion were assessed using ultrasonography.

Results: Overall accuracy of manual needle placement evaluated using ultrasonography was 51.2%. Accuracy was significantly higher for the finger flexors than for the wrist flexors (63.4% vs 39.0%). The finger flexors were significantly thicker than the wrist flexors (mean 1.58 vs 0.49 cm).

Conclusion: Instrumental guidance should be used in order to achieve an acceptable accuracy of needle placement when performing botulinum toxin type A injections into the forearms muscles of chronic stroke patients with spastic flexed wrist and clenched fist.

Key words: muscle hypertonia; hand; rehabilitation; upper extremity.

INTRODUCTION

Botulinum toxin type A (BoNT-A) is a first-line treatment for focal spasticity (1). Its ability to block acetylcholine release at the neuromuscular junction accounts for its therapeutic action (2). There is level A evidence supporting the effectiveness of BoNT-A for the treatment of upper limb spasticity (3). The major causes of loss of BoNT-A response in adult patients with focal spasticity are: inaccurate selection and identification of the correct muscle for injection, insufficient drug dosages, inadequate injection technique, development of changes in the muscle, and formation of neutralizing antibodies (4).

A recent study on adults with upper limb spasticity compared the effects of manual needle placement without instrumental guidance, electrical stimulation and ultrasonography-guided BoNT-A injection into the forearm muscles of chronic stroke patients, reporting that instrument-guided injections led to the largest clinical and analytical improvement in the treatment of spastic overactivity of the wrist and finger flexors (5). These findings are in keeping with the European consensus table on the use of BoNT-A in adult spasticity, which recommends injecting deep-seated and small muscles under instrumental guidance (4). Nevertheless, instrument-guided injections are not routinely carried out because of their procedural difficulty, the time required and differences in clinical settings, with a wide number of physicians using no instrumental guidance to deliver BoNT-A treatment (4–6).

Accurate injection into the target muscle is a key element for effective and safe BoNT-A treatment of muscle overactivity (7–14). The accuracy of needle insertion into the upper limb muscles without instrumental guidance has been studied in adults with dystonia and children with cerebral palsy (15, 16). There is a lack of evidence about the precision of BoNT-A injections that are not instrument-guided in adults with upper limb spasticity, which is further complicated by the fact that spastic muscles develop structural changes over time, with a disruption of normal anatomy (17, 18), and by the anatomical and physiological differences between children and adults.

The main aim of the current study was to investigate the accuracy of manual needle placement without instrumental guidance for BoNT-A injection into the forearm muscles of adult patients with spastic flexed wrist and clenched fist as a consequence of stroke. The secondary aim was to examine the muscle thickness of spastic wrist and finger flexors in adults with stroke.
METHODS

Inclusion criteria were as follows: age over 18 years, upper limb spasticity cura a consequence of first-ever ischaemic or haemorrhagic stroke (documented by a computerized tomography scan or magnetic resonance imaging; subarachnoid haemorrhage and transient ischaemic attack excluded), wrist and finger flexors tone graded at least 1+ on the modified Ashworth scale (MAS) (19), time from stroke onset at least 6 months and time from last BoNT-A treatment at least 5 months. Exclusion criteria were as follows: inclusion in other clinical trials, fixed contractures (tone graded 4 on the MAS) or bony deformities in the affected upper limb, previous treatment of the affected upper limb spasticity with neurolytic or surgical procedures, and other neurological or orthopaedic conditions involving the upper limbs. All patients gave their informed consent for participation in the study, which was carried out according to the principles of the Declaration of Helsinki and was approved by the ethics committee of the Department of Neurological and Movement Sciences of Verona University.

All subjects included in the current study were scheduled to receive BoNT-A injection into the following forearm muscles: flexor carpi radialis (FCR), flexor carpi ulnaris (FCU), flexor digitorum superficialis (FDS) and flexor digitorum profundus (FDP). Surface identification of the muscles to inject was performed according to the Huber & Heck’s atlas suggestions (20). The injection site was determined using palpation only, and the following anatomical landmarks: wrist joint, medial elbow epicondyle, radial styloid process, ulnar styloid process and ulnar border (20). The FCR injection site was marked at approximately 30% of the distance from the medial elbow epicondyle to the wrist joint (injection area one-third of the distance along a line connecting the medial epicondyle to the FCR tendon at the wrist) (20). The FCU injection site was marked at approximately 30% of the distance from the medial elbow epicondyle to the ulnar styloid process (injection area one-third of the distance along a line connecting the medial epicondyle to the ulnar styloid process) (20). The FDS was marked at 50% of the distance from the medial elbow epicondyle to the ulnar styloid process (injection area half of the distance between the medial elbow epicondyle and the line connecting the radial styloid process to the ulnar one) (20). The FDP was marked at 50% of the distance from the medial elbow epicondyle to the ulnar styloid process (injection area half of the distance between the ulnar border and the line connecting the medial epicondyle to the ulnar styloid process). With the forearm held in supination, the injections were carried out directly above the ulnar side (20). A board of clinicians with more than 3 years’ experience in treatment of spasticity performed all injections.

A physician with more than 6 years’ experience performed B-mode, real-time, ultrasonography of the affected forearm muscles using the Logiq® Book XP system (GE Medical Systems, Milwaukee, WI, USA) interfaced with a linear transducer (scanning frequency 10 MHz) to check the accuracy of needle placement (accurate injection = needle placed into the targeted muscle; no selection of FDS and FDP fascicles) and to measure muscle thickness (distance from the superficial to the deep aponeurosis) at each injection site (21). The transducer was positioned in the transverse view, perpendicular to the muscle surface and placed gently on the skin using water-soluble transmission gel to avoid any pressure-induced alteration of the muscle tissue dimensions (22). If the needle was not placed into the targeted muscle, it was correctly repositioned under ultrasonographic guidance before injecting BoNT-A. All patients remained in the supine position with their affected arm as straight as possible during the whole procedure.

The Fisher’s exact test and the Student’s t-test were used to assess the effect of age (≤ 65 vs > 65 years), sex (male vs female), time from onset (≤ 2 vs > 2 years), MAS at wrist (≤ 2 vs > 2 points) and fingers (≤ 2 vs > 2 points) on the accuracy of needle placement (accurate vs inaccurate) and muscle thickness. Pearson’s analysis was performed to determine the correlation between the accuracy of needle placement and muscle thickness. Binary logistic regression was used to compute adjusted odds ratios and 95% confidence intervals to investigate the effects of age, sex, time from onset, MAS at wrist and fingers on the accuracy of needle placement (coded as 1 = accurate and 0 = inaccurate).

The significance level was p < 0.05. Statistical analysis was carried out using the SPSS version 21.0 software (SPSS Inc, Chicago, USA).

RESULTS

Forty-one adults (24 males and 17 females; mean age 62.6 years, standard deviation (SD) 13.5) with spastic flexed wrist and clenched fist (median spasticity severity on the MAS: 3, interquartile range 2–3; mean time from last BoNT-A treatment: 6.1 months (SD 0.4)) as a consequence of stroke (mean time from stroke onset: 3.2 years (SD 1.3)) were recruited from among 113 outpatients consecutively admitted to the Neurological Rehabilitation Unit of the Azienda Ospedaliera

Table 1. Effect of age, sex, time from onset and spasticity on the overall accuracy of needle placement and muscle thickness

<table>
<thead>
<tr>
<th>Parameter</th>
<th>FCR (n=41)</th>
<th>FCU (n=41)</th>
<th>FDS (n=41)</th>
<th>FDP (n=41)</th>
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<tbody>
<tr>
<td>Age</td>
<td></td>
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<tr>
<td>≤ 65 years (n = 21)</td>
<td>33.3 (%), 0.59 (0.33)</td>
<td>33.3 (%), 0.33 (0.25)</td>
<td>61.9 (%), 1.25 (0.45)</td>
<td>66.7 (%), 1.71 (0.49)</td>
</tr>
<tr>
<td>&gt; 65 years (n = 20)</td>
<td>50.0 (%), 0.69 (0.24)</td>
<td>40.0 (%), 0.34 (0.27)</td>
<td>60.0 (%), 1.46 (0.49)</td>
<td>65.0 (%), 1.90 (0.46)</td>
</tr>
<tr>
<td>Sex</td>
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<tr>
<td>Male (n = 24)</td>
<td>52.4 (%), 0.63 (0.30)</td>
<td>47.6 (%), 0.37 (0.27)</td>
<td>71.4 (%), 1.42 (0.48)</td>
<td>71.4 (%), 1.84 (0.45)</td>
</tr>
<tr>
<td>Female (n = 17)</td>
<td>30.0 (%), 0.65 (0.24)</td>
<td>25.0 (%), 0.29 (0.24)</td>
<td>50.0 (%), 1.28 (0.48)</td>
<td>60.0 (%), 1.77 (0.52)</td>
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<tr>
<td>Time from onset</td>
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<tr>
<td>≤ 2 years (n = 12)</td>
<td>58.3 (%), 0.73 (0.30)</td>
<td>41.7 (%), 0.36 (0.29)</td>
<td>75.0 (%), 1.27 (0.36)</td>
<td>58.3 (%), 1.72 (0.54)</td>
</tr>
<tr>
<td>&gt; 2 years (n = 29)</td>
<td>34.5 (%), 0.60 (0.29)</td>
<td>34.5 (%), 0.32 (0.25)</td>
<td>55.2 (%), 1.38 (0.52)</td>
<td>69.0 (%), 1.84 (0.46)</td>
</tr>
<tr>
<td>MAS wrist</td>
<td></td>
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<td></td>
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<tr>
<td>≤ 2 (n = 17)</td>
<td>29.4 (%), 0.64 (0.29)</td>
<td>35.3 (%), 0.28 (0.22)</td>
<td>58.8 (%), 1.48 (0.53)</td>
<td>82.4 (%), 2.04 (0.39)*</td>
</tr>
<tr>
<td>&gt; 2 (n = 24)</td>
<td>50.0 (%), 0.64 (0.30)</td>
<td>37.5 (%), 0.37 (0.28)</td>
<td>62.5 (%), 1.62 (0.42)</td>
<td>54.2 (%), 1.64 (0.47)*</td>
</tr>
<tr>
<td>MAS fingers</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 2 (n = 16)</td>
<td>43.8 (%), 0.59 (0.26)</td>
<td>25.0 (%), 0.33 (0.26)</td>
<td>62.5 (%), 1.34 (0.44)</td>
<td>56.3 (%), 1.79 (0.58)</td>
</tr>
<tr>
<td>&gt; 2 (n = 25)</td>
<td>40.0 (%), 0.68 (0.31)</td>
<td>44.0 (%), 0.34 (0.25)</td>
<td>60.0 (%), 1.36 (0.51)</td>
<td>72.0 (%), 1.81 (0.41)</td>
</tr>
</tbody>
</table>

*p < 0.05. FCR: flexor carpi radialis; FCU: flexor carpi ulnaris; FDS: flexor digitorum superficialis; FDP: flexor digitorum profundus; SD: standard deviation; MAS: Modified Ashworth Scale.
The main aim of the present study was to investigate the accuracy of manual needle placement without instrumental guidance, evaluated using ultrasonography, when injecting BoNT-A into the forearm muscles of adults with spastic flexed wrist and clenched fist as a consequence of stroke. The results indicate an overall accuracy of 51.2% for not instrument-guided injections into the spastic forearm muscles evaluated in the current study, with a significantly higher precision for the finger flexors than for the wrist flexors (63.4% vs 39.0%). In particular, the accuracy of manual needle placement without instrumental guidance was 41.5% for the FCR, 36.6% for the FCU, 61.0% for the FDS and 65.9% for the FDP.

The accuracy of needle placement into the targeted muscle is a crucial issue in the treatment of focal spasticity with BoNT-A (4). With regard to the localization of forearm muscles for BoNT-A treatment in adult patients with upper limb spasticity, Henzel et al. (23) observed that ultrasonography locates FCR, FDS, pronator teres and flexor pollicis longus at distinctly different sites compared with those suggested by surface identification. This is probably because the anatomical landmarks were originally based on cadaveric studies of people with upper limbs positioned in full extension and supination (23, 24). Furthermore spastic muscles have been reported to develop a progressive disruption of tissue architecture including atrophy (loss of muscle mass), loss of sarcomeres (shortening), accumulation of intramuscular connective tissue and increased fat infiltration (17, 18, 22). It is plausible that a distortion of the normal three-dimensional muscle structure would lead to a mismatch between anatomical landmarks and actual muscle location in patients with spasticity, with a consequent reduction in accuracy in muscle localization based on surface measurements (23). Our findings about the impact of muscle thickness on the accuracy of needle placement are in keeping with this hypothesis. Indeed, the accuracy of needle insertions performed without instrumental guidance was observed to have a significant direct correlation with the actual thickness of each muscle examined in the current study. Thus, considering that muscle thickness was found to relate to muscle atrophy (25), the current results further confirm that the disruption of normal anatomy in spastic muscles due to progressive structural changes plays an important role in reducing the accuracy of muscle localization by means of surface identification (23).

For adults with overactivity of upper limb muscles, the precision of not instrument-guided BoNT-A injections has been evaluated in a sample of 14 patients with focal hand dystonia, and been shown to have an overall accuracy of 38% for needle placement into the forearm flexor muscles (a total of 38 injections were evaluated) (15). In particular, Mollov et al. (15) found that the accuracy of manual needle placement without instrumental guidance, evaluated using electromyography (EMG), was 66.6% for the FCR (3 injections evaluated), 50% for the FCU (4 injections evaluated), 16.6% for the FDS (6 injections evaluated) and 55.5% for the FDP (9 injections evaluated). These observations are not in agreement with our findings, probably because of large differences between the 2 studies in terms of the total number of needle placements examined (38 vs 164 injections) and the muscles injected (FCR: 3 vs 41 injections; FCU: 4 vs 41 injections; FDS: 6 vs 41 injections; FDP: 9 vs 41 injections). With regard to patients with upper limb spasticity, the accuracy of BoNT-A injection without instrumental guidance was checked against electrical stimulation on a sample of 226 children with cerebral palsy, and an accuracy of 13% was observed for the FCR (30 injections evaluated) and 16% for the FCU (56 injections evaluated) (16). These findings are not in agreement with our results, probably because of the differences in muscle anatomy and physiology between paediatric and adult patients.

### DISCUSSION

The main aim of the present study was to investigate the accuracy of manual needle placement without instrumental guidance, evaluated using ultrasonography, when injecting BoNT-A into the forearm muscles of adults with spastic flexed wrist and clenched fist as a consequence of stroke. The results indicate an overall accuracy of 51.2% for not instrument-guided injections into the spastic forearm muscles evaluated in the current study, with a significantly higher precision for the finger flexors than for the wrist flexors (63.4% vs 39.0%). In particular, the accuracy of manual needle placement without instrumental guidance was 41.5% for the FCR, 36.6% for the FCU, 61.0% for the FDS and 65.9% for the FDP.

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### Table II. Multivariate logistic model of covariates influencing the accuracy of needle placement

<table>
<thead>
<tr>
<th>Parameter</th>
<th>OR</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, ≤65 vs &gt; 65 years</td>
<td>2.658</td>
<td>0.583–12.121</td>
<td>0.207</td>
</tr>
<tr>
<td>Sex, male vs female</td>
<td>0.329</td>
<td>0.078–1.383</td>
<td>0.129</td>
</tr>
<tr>
<td>Time from stroke, ≤2 vs &gt; 2 years</td>
<td>0.422</td>
<td>0.094–1.896</td>
<td>0.260</td>
</tr>
<tr>
<td>MAS wrist, ≤2 vs &gt; 2 points</td>
<td>3.583</td>
<td>0.730–17.582</td>
<td>0.116</td>
</tr>
<tr>
<td>MAS fingers, ≤2 vs &gt; 2 points</td>
<td>1.055</td>
<td>0.247–4.512</td>
<td>0.942</td>
</tr>
</tbody>
</table>

Accurate injection coded as 1; inaccurate injection coded as 0. OR: odds ratio; CI: confidence interval; MAS: Modified Ashworth Scale.

Universitaria Integrata of Verona, Italy. The enrolment period was from January 2012 to December 2013. In total, 164 needle insertions into the forearm muscles (41 injections into each of the following muscles: FCR, FCU, FDS and FDP) were evaluated.

The overall accuracy of manual needle placement without instrumental guidance evaluated using ultrasonography was 51.2%. In particular, it was significantly higher ($p = 0.002$) for the finger flexors than for the wrist flexors (63.4% vs 39.0%). No difference was found as to the accuracy for the FCR vs FCU as well as for the FDS vs FDP comparisons. The accuracy of manual needle placement without instrumental guidance, evaluated using ultrasonography, for each of the forearm muscles evaluated in the current study was defined as follows: FCR 41.5%, FCU 36.6%, FDS 61.0% and FDP 65.9%.

Muscle thickness was significantly higher ($p < 0.001$) at the finger flexors than the wrist flexors (mean 1.58 cm (SD 0.53) vs 0.49 cm (SD 0.32)). With regard to the wrist flexors, the FCR was significantly thicker ($p < 0.001$) than the FCU (mean 0.65 cm (SD 0.30) vs 0.34 cm (SD 0.26)). With regard to the finger flexors, muscle thickness was significantly higher ($p < 0.001$) at the FDP than the FDS (mean 1.81 cm (SD 0.49) vs 1.35 cm (SD 0.48)). The effects of age, sex, time from stroke onset and spasticity on the overall accuracy of needle placement and muscle thickness are shown in Table I.

A significant direct correlation was found between the accuracy of manual needle placement without instrumental guidance and the actual thickness of the FCR ($p < 0.001$; $p = 0.705$), FCU ($p < 0.001$; $p = 0.803$), FDS ($p = 0.005$; $p = 0.433$) and FDP ($p = 0.020$; $p = 0.363$). The binary logistic regression analysis of covariates influencing the accuracy of needle placement is reported in Table II.
**Study limitations**

The current study has several limitations. First, the sample size was relatively small. The population size may have hindered the evaluation of differences in the accuracy of manual needle placement without instrumental guidance for comparisons of FCR vs FCU and FDS vs FDP. Secondly, no fascicles selection was attempted during the treatment of FDS and FDP. This may have led to an overestimation of the accuracy of needle placement into the finger flexors, which may be lower with regard to the targeting of specific fascicles of these muscles. Localization of each fascicle of the FDS and FDP is important to ensure an effect on each digit. However, the main objective of the current study was not to compare the effects of different injection techniques in the treatment of upper limb spasticity, but to investigate the accuracy of not instrument-guided BoNT-A injections into the spastic forearm muscles. This was mainly because manual needle placement without instrumental guidance is widely used to inject BoNT-A into the wrist and finger flexors, despite the fact that it is not recommended for treating small and deep-seated muscles. Thus, the outcome chosen was the accuracy of needle placement into (every part of) the targeted muscle and its thickness, not taking into account the selection of fascicles. Thirdly, there is a lack of comparison between the accuracy of manual needle placement without instrumental guidance and EMG/electrical stimulation-guided approaches. This was because ultrasonography is the only tool that enables checking of the accuracy of intramuscular BoNT-A injections as well as examination of muscle thickness, which were the aims of the current study. Furthermore, considering that we used ultrasonography only to perform anatomical evaluations, we are confident that its operator dependence did not affect our findings. Fourthly, we studied only a single injection site for each muscle. Fifthly, we did not evaluate the thickness of subcutaneous tissue. Future studies are required involving a larger population and other muscles, such as brachioradialis, brachialis, biceps brachii, pronator teres, pronator quadratus, and flexor pollicis longus, which contribute to the main clinical patterns of upper limb spasticity.

**REFERENCES**