Use of surface EMG for evaluation of upper limb spasticity during botulinum toxin therapy in stroke patients

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Summary

The clinical assessment of spasticity in stroke patients generally includes descriptive scales, such as the Modified Ashworth Scale (MAS) and the Global Pain Scale (GPS), however these may not be sufficiently sensitive to accurately detect improvements, especially at upper limb level; electromyography (EMG) may be the answer to this clinical requirement.

The aim of this study was to quantify the effects of botulinum toxin type A (BTX) in treating upper extremity spasticity in stroke patients, using clinical evaluation (MAS and GPS) and EMG.

Ten patients were assessed before, 30 days and 180 days after BTX injection using clinical evaluations and EMG. At 30 days all clinical measures improved significantly. Whereas MAS scores, after recording an improvement at the first evaluation session, were worse at the second assessment, GPS scores improved over time, both at the first and at the second evaluation session. A reduction of EMG activity was found 30 days after injections, in particular at baseline and during passive flexion movement. Our results demonstrated that measurement of EMG activity may be an effective means of detecting functional improvements and of monitoring the effects of treatment in post-stroke patients.

KEY WORDS: botulinum toxin, electromyography, spasticity, stroke, upper limb

Introduction

Stroke, a major cause of disability involving the upper and lower limbs (1), results in the development of upper motor neuron syndrome (UMNS). This syndrome is commonly associated with spasticity and muscle overactivity, which can lead to abnormal limb posturing, interfering with active and passive function. The origin of the limb deformity in patients with UMNS lies in the concept of unbalanced agonist and antagonist muscle forces acting across joints. Botulinum toxin type A (BTX) is a pharmacological treatment that modifies muscle force and, hence, can treat muscle imbalance. Intramuscular BTX has been demonstrated to be a safe and effective treatment for reducing disability in patients with severe upper limb spasticity, such as those with stroke (2,3). BTX binds to the presynaptic membranes of cholinergic motor neurons and, once internalised, cleaves components of the cell’s exocytic machinery, preventing the discharge of acetylcholine-containing vesicles and hence neurotransmission at the neuromuscular junction (4-6). Consequently, injection of BTX into selected muscles produces dose-dependent chemical denervation resulting in reduced muscular activity lasting about 12-16 weeks (7,8).

BTX therapy offers benefits to selected patients, by enhancing the efficacy of physical therapy programmes, even though the question of whether it significantly improves functional parameters is still debated. Indeed, the literature lacks homogeneous indications on what is the most accurate method for assessing the effects of BTX therapy. The efficacy of BTX is sometimes demonstrated in terms more of its reduction of muscle tone than its effect on active functional goals (2,9-13), while Pandyan et al. (14) found that the Modified Ashworth Scale (MAS) was unable to detect the therapeutic improvement. In short, it was noticed that the measures employed may not be sensitive enough to detect focal improvements (15): although they can highlight gains in one or two important items, since a large number of irrelevant items do not change, these gains are lost in the overall scores. Moreover, Bakheit et al. (8) observed that several aspects related to stroke, such as the size of the affected area, neglect, anosognosia, and other aspects of cognition can confound the results of the evaluation. Recently, Turner-Stokes et al. (16) suggested using goal attainment scaling to assess functional limitation in patients treated with BTX (17). According to these considerations, it is important, from a clinical point of view, to have an accurate method of assessing spasticity, and the evaluation of muscle activation using EMG may be the answer to this need. Dynamic EMG provides timing and action data for the muscles that are the prime movers of body segments and bones: understanding the activity of muscles is crucial to a better understanding of
the root causes of movement abnormalities. EMG evaluation can highlight muscular activity at rest (hypertonus) and may shed light on the functional relationship between agonist and antagonist muscles.

Some studies in the literature have investigated the value of EMG in the assessment of the effects of BTX in stroke patients, comparing it to other clinical evaluations. Cousins et al. (18), in two case reports, described two patients assessed over 20 weeks after BTX injection for post-stroke spasticity focusing on clinical (MAS) and neurophysiological (EMG of biceps and triceps, the long wrist and finger flexor and extensor muscles) measures. They found that the MAS and EMG results were not consistent due to the different constructs of the two measures. They demonstrated that while MAS is an inadequate method for identifying spasticity and for evaluating the effects of the medication, EMG is a satisfactory tool for identifying and monitoring spasticity and the effects of treatments. Pandyan et al. (14) quantified the clinical efficacy of BTX in treating elbow flexor spasticity in a stroke population. They evaluated spasticity with the MAS and surface EMG; strength at the elbow, grip strength and upper limb function (Action Reaching Arm Test) were also assessed. They found that spasticity (as measured by flexor EMG activity) was reduced after treatment but the MAS was unable to detect this improvement.

It is clear from the literature that most studies investigating the effects of BTX on the upper limb in stroke patients were conducted using clinical and functional scales and in very small numbers of patients, while few also used EMG recordings. In view of the clinical need to investigate this topic in more depth, the aim of this study was to assess and quantify the effects of BTX injection in treating upper extremity spasticity in stroke patients, comparing it to other clinical evaluations for surface EMG were followed. The common criteria for assessing spasticity include the Modified Ashworth Scale (MAS) and EMG activity assessments were conducted. The MAS clinically assesses muscle spasticity based on the evaluation of resistance to spastic muscle mobilization (0=no increase in tone; 4=maximum muscle rigidity during flexion-extension movement) (20).

During the evaluation, the patients sat in a comfortable position in front of a desk with the paretic limb elbow resting on the desk at 90 degrees and the wrist in a neutral position.

The measures were taken in three different conditions: i) at rest: starting from the starting position described above, the individuals were asked to maintain this status for 10 seconds; ii) during active extension and flexion of the left wrist: starting from the starting position, the patients were asked to execute five repetitions of wrist maximal extension (AE: active extension) followed by five repetitions of wrist maximal flexion (AF: active flexion) at self-selected speed with breaks between the repetitions; iii) during passive extension and flexion of the left wrist: starting from the starting position a trained physical therapist manually moved the wrist slightly from the neutral position to maximal possible extension (five repetitions; PE: passive extension); after a break, the same physical therapist manually moved the wrist slightly from the neutral position to maximal possible flexion (five repetitions; PF: passive flexion) (19).

In all three conditions, MAS, Global Pain Scale (GPS) and EMG activity assessments were conducted. The MAS clinically assesses muscle spasticity based on the evaluation of resistance to spastic muscle mobilization (0=no increase in tone; 4=maximum muscle rigidity during flexion-extension movement) (20).

The GPS is a visual analogue scale used to determine the severity of spasticity-related pain (0=no pain; 100=maximum pain).

The subjects’ clinical and demographic data at T0 are reported in Table I.

For the EMG recording, pairs of bipolar Ag/AgCl surface electrodes with a diameter of 10 mm and an inter-electrode spacing of 22 mm were placed on clean, shaven skin overlying the flexor and extensor carpi radialis of the spastic upper limb. As regards electrode placement, the SENIAM (21) recommendations for surface EMG were followed. The common

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**Materials and methods**

A longitudinal study design with three repeated measures, before (T0), at 30 days (T30) and at 180 days (T180) after BTX injection, was used.

Ten paretic patients (7 females, 3 males; mean age: 63.6 years; SD: 14.79) were selected according to the following criteria: right-handed, presence of left-side spasticity after stroke (dating back not more than five years), no previous pharmacological treatment with BTX, no other current therapy for spasticity, and the presence of a spastic posture of the forearm characterised by flexion of the elbow, wrist and fingers.

The subjects were volunteers and they gave their written informed consent to participate in this research, in accordance with local ethics committee requirements. All patients received injections of BTX type A (Botox, Allergan Ltd, UK) to the biceps brachii (mean dose 100 U), flexor carpi radialis (mean dose 50 U) and flexor digitalis profundus (mean dose 50 U) muscles. Only the left side was treated. The injections were placed in the muscle using anatomical landmarks as in the routine EMG examination; EMG was not used in this study.

During the evaluation, the patients sat in a comfortable position in front of a desk with the paretic limb elbow resting on the desk at 90 degrees and the wrist in a neutral position.

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**Table I - Subjects’ clinical and demographic data at T0**

<table>
<thead>
<tr>
<th># subject</th>
<th>Sex</th>
<th>Age (years)</th>
<th>Time since stroke (years)</th>
<th>MAS (0-4)</th>
<th>GPS (0-100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>63</td>
<td>3</td>
<td>3</td>
<td>30</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>69</td>
<td>5</td>
<td>3</td>
<td>40</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>73</td>
<td>2</td>
<td>4</td>
<td>20</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>76</td>
<td>3</td>
<td>3</td>
<td>30</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>51</td>
<td>3</td>
<td>3</td>
<td>20</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>88</td>
<td>6</td>
<td>3</td>
<td>20</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>56</td>
<td>6</td>
<td>4</td>
<td>60</td>
</tr>
<tr>
<td>8</td>
<td>F</td>
<td>61</td>
<td>3</td>
<td>4</td>
<td>60</td>
</tr>
<tr>
<td>9</td>
<td>F</td>
<td>65</td>
<td>3</td>
<td>3</td>
<td>40</td>
</tr>
<tr>
<td>10</td>
<td>F</td>
<td>34</td>
<td>1</td>
<td>3</td>
<td>40</td>
</tr>
</tbody>
</table>

Abbreviations: MAS=Modified Ashworth Scale; GPS=Global Pain Scale.
reference electrode was positioned on the dorsal surface of the hand. The ground electrode was placed over the tibial tuberosity. EMG signals were sampled at 1500 Hz and raw signals were amplified and bandpass-filtered (10-500 Hz). EMG amplitudes (root mean squared values, RMSs) were also calculated from EMG signals.

To ensure reproducibility of the acquisition technique and to avoid the introduction of errors due to different operators, the clinical evaluation and electrode positioning were always performed by the same two experienced operators (one performing the clinical assessment and one the electrode positioning).

All the previously defined measures (MAS, GPS and RMSs) were computed for each subject; thereafter, the mean values and standard deviations of all the measures were calculated for the entire group in each evaluation (T0, T30 and T180). In this study, only the left side of each patient was considered.

A repeated measures one-way analysis of variance (ANOVA) was used to evaluate changes in clinical measures (MAS and GPS evaluation) and EMG activity (RMSs) as a function of time in the group. The post-hoc Newman-Keuls test was used to assess significant differences. Statistical significance was set at p< 0.05.

Results

There emerged no BTX-related serious adverse events or changes in safety profile, indicating that the BTX injections were well tolerated.

All the patients were able to complete both assessments (clinical and instrumental) in the three evaluation sessions (T0, T30 and T180).

Table II shows the results of the patients’ clinical assessments in the three sessions. At T30 both the MAS and the GPS showed significant improvements, which were close to 32% and 24% respectively; at T180, the MAS showed a return to the baseline value indicating a general increase in spasticity; conversely, the GPS value decreased significantly, this measure therefore displaying an improvement over time.

The results showed a significant decrement of average integrated EMG (RMSs) (Tables III and IV, over) 30 days after BTX injections (T30) in both extensor and flexor carpi radialis muscles, in particular at baseline and during passive flexion movement. The improvements at baseline were close to 50% for the extensor and 49% for the flexor muscles; during passive flexion the changes were respectively 40% and 36% (Fig. 1, over).

No significant changes were found at T180 in any condition, denoting a global maintenance of T30 EMG activity.

Table II - Mean values (+ standard deviation) of clinical measures of the evaluated group at the three assessments

<table>
<thead>
<tr>
<th>Clinical measures</th>
<th>T0</th>
<th>T30</th>
<th>T180</th>
<th>F</th>
<th>df</th>
<th>effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAS, 0-4</td>
<td>3.3±0.5</td>
<td>2.4±0.5*</td>
<td>2.9±0.5**</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GPS, 0-100</td>
<td>36.0±14.4</td>
<td>22.0±12.5*</td>
<td>17.0±12.5***</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations and symbols: MAS=Modified Ashworth Scale; GPS=Global Pain Scale. *=p-value < 0.05 for the comparisons T0 vs T30 and T0 vs T180; **=p-value < 0.05, for the comparison T30 vs T180.

Table III - Root mean square (RMS) values of flexor carpi radialis EMG signals

<table>
<thead>
<tr>
<th>NEUTRAL (mV)</th>
<th>T0</th>
<th>T30</th>
<th>T180</th>
<th>F</th>
<th>df</th>
<th>effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>PE (mV)</td>
<td>0.021 ± 0.012</td>
<td>0.011 ± 0.006*</td>
<td>0.013 ± 0.005*</td>
<td>2.186</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>AE (mV)</td>
<td>0.055 ± 0.020</td>
<td>0.048 ± 0.023</td>
<td>0.051 ± 0.026</td>
<td>0.121</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>AF (mV)</td>
<td>0.035 ± 0.024</td>
<td>0.028 ± 0.016</td>
<td>0.031 ± 0.013</td>
<td>1.108</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>PF (mV)</td>
<td>0.061 ± 0.034</td>
<td>0.057 ± 0.019</td>
<td>0.056 ± 0.034</td>
<td>0.251</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.024 ± 0.015</td>
<td>0.015 ± 0.006*</td>
<td>0.018 ± 0.015*</td>
<td>2.940</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations and symbols: PE=passive extension; AE=active extension; AF=active flexion; PF=passive flexion, of the wrist in the evaluated group. *=p-value < 0.05, in the comparisons T0 vs T30 and T0 vs T180.

Table IV - Root mean square (RMS) values of extensor carpi radialis EMG signals

<table>
<thead>
<tr>
<th>NEUTRAL (mV)</th>
<th>T0</th>
<th>T30</th>
<th>T180</th>
<th>F</th>
<th>df</th>
<th>effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>PE (mV)</td>
<td>0.012 ± 0.010</td>
<td>0.006 ± 0.004*</td>
<td>0.007 ± 0.003*</td>
<td>2.278</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>AE (mV)</td>
<td>0.021 ± 0.006</td>
<td>0.019 ± 0.007</td>
<td>0.020 ± 0.009</td>
<td>0.284</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>AF (mV)</td>
<td>0.053 ± 0.030</td>
<td>0.049 ± 0.029</td>
<td>0.054 ± 0.035</td>
<td>0.977</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>PF (mV)</td>
<td>0.044 ± 0.022</td>
<td>0.039 ± 0.028</td>
<td>0.038 ± 0.021</td>
<td>0.432</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.026 ± 0.012</td>
<td>0.016 ± 0.006*</td>
<td>0.018 ± 0.009*</td>
<td>2.967</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations and symbols: PE=passive extension; AE=active extension; AF=active flexion; PF=passive flexion, of the wrist in the evaluated group. *=p-value < 0.05, in the comparisons T0 vs T30 and T0 vs T180.
Finally, it is important to note that the improvements in EMG activity were stronger than those recorded in the clinical evaluations.

Discussion

The present study documented the progress of a group of patients with upper limb spasticity secondary to stroke undergoing treatment with BTX. Spasticity is currently evaluated by clinical scales which are generally rapidly administered; however, the evidence provided by clinical measures of spasticity has been shown to be limited, especially after BTX treatment (18). With this therapy, unlike others for spasticity (oral or intrathecal), the benefit is not continuous; instead it generally shows a peak effect, followed by a plateau and then a progressive disappearance; moreover, its action is selective, only affecting the segments of the body connected to the treated muscle. Whereas gait analysis integrated with surface EMG is the standardised approach for evaluating the spastic lower limb, the question of the most opportune method for evaluating the spastic upper limb is still debated. This dilemma is justified by the biomechanical diversity of the upper limb and by its variety of motor functions, potential targets for analysis, compared with the single predominant locomotor function of the lower limb. For this reason, there is a clinical need for more accurate assessment of the upper limb. In this context, evaluation of muscle activity using EMG could play a key role in quantifying the efficacy of BTX, an antispastic medication.

In this study, 10 patients with upper limb spasticity after stroke were evaluated in a longitudinal study design at three assessments, before (T0) and 30 days (T30) and 180 days (T180) after BTX injection. These assessments were based on clinical evaluations (MAS, GPS) and EMG activity. The results of this study indicate that BTX reduced upper limb spasticity in our patients. Treatment with BTX markedly decreased the muscular activity of the spastic limb; this effect ends, on average, within six months, although it can last longer (2, 8, 18, 22).

From the clinical evaluations there emerged a common trend at T30, when both MAS and GPS scores were found to be significantly improved. At T180 the results were not consistent: the MAS score worsened significantly, returning to the baseline value, while the GPS value decreased, demonstrating a continuous reduction of pain after BTX injection over time, probably due to a central reorganisation of pain control (23, 24).

As regards the EMG signal, significant reductions in flexor and extensor muscle spasticity were found at T30, especially at rest and during passive flexion, and these improvements were maintained at T180, too. Meanwhile, it is important to note that evaluation of the EMG signal during the execution of the other movements revealed a slight reduction in spasticity at T30.

As shown by our results, the two spasticity measures (MAS and EMG) gave consistent results at short-term follow up (T30), demonstrating a general improvement. On the contrary, at T180 the results were not consistent: while MAS worsened, the results of the EMG demonstrated the maintenance over time of the spasticity reduction recorded at T30. Thus, at T180, while the semi-quantitative evaluation of tone would seem to indicate the reappearance of spasticity, the quantitative EMG evaluation clearly indicated maintenance of the positive effects, suggesting that the next BTX administration could be postponed.

In addition our data highlighted that at T30 the degree of improvement as shown by EMG data was much more marked than that shown by the MAS score (MAS improvement: 32%; EMG activity improvement: 50% for the extensor and 49% for the flexor carpi radialis at baseline; 40% for the extensor and 36% for the flexor carpi radialis during passive flexion), supporting the idea that the rating scales used were poorly sensitive for detecting functional improvement.

We also found that muscle extensor activities were reduced, probably because the effects of BTX on flexor muscles favour the physical activity approach, resulting in an improvement of the activity of the entire muscle segment.

In conclusion, the lack of correspondence between the MAS scores and EMG activity found in this study supports previous observations that MAS, in contrast to EMG, may not be a valid measure of spasticity (14, 18). This could be due to the different constructs of the two evaluations: MAS is a measure of resistance to passive movement, while EMG quantifies levels of muscle activity and is a direct measure of spasticity. Thus, MAS could lack sensitivity and may be an incomplete tool for identifying spasticity and monitoring the effects of treatment, especially over time. On the contrary, the EMG...
evaluation, which is a neurophysiological measure of spasticity, may be a valuable clinical tool for detecting these aspects in post-stroke patients. This result is a significant cause for concern, as the MAS is the measure generally used in clinical practice for evaluating the efficacy of antispastic medication. According to these results, the EMG evaluation proved able to assess, in a non-invasive and precise way, the muscular contribution to a dynamic deformity and the effects of BTX on the muscle activity over time. This neurophysiological measure of spasticity could assist clinicians in diagnostic processes and thus direct treatment strategies.

This study has some limitations. The small number of participants resulted in limited strength of the clinical and statistical findings, and the absence of a control group made it impossible to assess the degree to which the observed changes might be associated with a placebo effect (14). However our results support previous observations. Difficulties in measuring EMG signals include ensuring that skin impedance or placement of EMG electrodes is identical between participants and over all sessions. We could not eliminate differences in the amplitudes of the signals from the surface EMG electrodes at different evaluations, but this problem was minimised by ensuring that the standard procedure described by SENIAM was followed and by using the same operator for each EMG collection assessment.

References