Letters to the Editor

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Letter by Munin et al Regarding Article, “Botulinum Toxin for the Upper Limb After Stroke (BoTULS) Trial: Effect on Impairment, Activity Limitation, and Pain”

To the Editor:

We read the article by Shaw et al1 with great interest. Their trial examined whether abobotulinumtoxinA and task practice therapy could improve upper limb function after spastic hemiparesis more than therapy alone in controls based on changes in the Action Research Arm Test (ARAT).1 There are several points that may explain why the investigators saw only improvements in patient-rated basic upper limb functional activities rather than observed ARAT scores in treated subjects.

When injecting botulinum toxin, the clinicians used surface localization to identify forearm muscles instead of more accurate guidance from ultrasound with electromyography or nerve stimulation. We demonstrated that ultrasound guidance during botulinum toxin injections is more accurate than surface localization when targeting forearm muscles that have a complex pattern of overlapping anatomy with superficial and deep layers.2 Using ultrasound guidance, muscles with several bellies (eg, flexor digitorum superficialis) can be administered doses individually to target specific spastic patterns in each belly. Confirmation of accurate drug placement can be attained by targeting end plate regions or visually ensuring that the injectate stays within fascial borders, and not by assuming that local diffusion of toxin would be sufficient for delivery.

The methodology was also hindered by using low median doses of abobotulinumtoxinA between 200 and 300 total units. In previous upper limb stroke spasticity studies, mean doses ranged between 500 and 1000 units.3 The majority of subjects had spasticity affecting the shoulder, elbow, wrist, and hand, indicating that many muscles required treatment. Although up to 9 different muscles could be injected based on clinical assessment, the median reported dose per individual muscle was ~100 units, meaning that only a few muscles were injected during a session. Because functional improvement was the primary outcome of this trial, inaccurate placement of toxin combined with suboptimal dosing of limited numbers of muscles may explain why the intervention group did not show improvement in ARAT relative to controls.

The Botulinum Toxin for the Upper Limb After Stroke study enrolled a majority of subjects with very low, if any, distal hand function at baseline (ARAT score, 0–3). Participants in the Botulinum Toxin for the Upper Limb After Stroke trial with some retained active upper limb function (ARAT score, 4–56) were more likely to experience a predefined successful outcome compared to the larger number of participants with no retained upper limb function (ARAT score, 0–3). Therefore, with severe baseline weakness in a majority of subjects, it is not surprising that botulinum toxin injections that block neuromuscular transmission and cause selective muscle weakening did not improve active functional movement as measured by the ARAT.

Measuring upper limb function is clearly more difficult than studying a more precisely defined construct like blood pressure. The authors of the article1 note that ~30% of subjects had improved ARAT scores at 3 months, although toxin injections did not affect this relationship. Our findings also demonstrated a gain in ARAT scores at 3 months in subjects administered a combination of onabotulinumtoxinA and task practice training, with and without functional electric stimulation.4 In the Botulinum Toxin for the Upper Limb After Stroke trial, significantly more abobotulinumtoxinA patients had improvement in subject-reported daily tasks, like opening the palm for cleaning and cutting nails and putting an arm through a coat sleeve. These findings indicate that different measures give us different information about the effectiveness of interventions on upper limb function and pose the question, which measures are best for measuring changes in upper limb spasticity after stroke? We appreciate the investigators’ contribution to the literature with this large, multicenter, randomized trial, and we hope that our comments further the discussion.

Disclosure

None.

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