Upper Extremity Spasticity in Children With Cerebral Palsy: A Randomized, Double-Blind, Placebo-Controlled Study of the Short-Term Outcomes of Treatment With Botulinum A Toxin

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Purpose Botulinum A toxin (BoNT-A) injections are used widely to manage lower extremity spasticity in children with cerebral palsy. However, their use in the upper extremity is less well defined. This randomized, double-blind, placebo-controlled clinical trial evaluated the safety and efficacy of upper extremity intramuscular injections of BoNT-A in a cross-section of children with varying levels of function.

Methods Upper extremity function of study participants (N = 73; M:F = 47:26; age range, 3–18 y) was evaluated using the House Classification system (scores, 0–8, where a higher score indicates higher functional ability). Three groups of children were identified based on their House scores: 0–2 (n = 10), 3–5 (n = 54), and 6–8 (n = 9). Following randomization, children received a BoNT-A or placebo injection at baseline. Injections were administered at 8 and 20 weeks if clinically indicated. Occupational therapists evaluated study participants at screening, at baseline, and at 4, 8, 14, 20, and 26 weeks. Physician evaluations occurred at baseline and at 8, 20, and 26 weeks. The Melbourne Assessment of Unilateral Upper Limb Function evaluated the quality of upper extremity function before and after injections and served as the primary outcome variable.

Results The majority of study participants underwent 3 injection sessions. Muscles injected were individualized based on each child's particular spasticity pattern. A statistically higher percentage of children receiving BoNT-A injections showed an improvement in the Melbourne assessment at 26 weeks compared with the children receiving placebo. The range, frequency, and severity of postinjection adverse events were similar in both groups.

Conclusions Children receiving BoNT-A injections demonstrated clinically meaningful short-term improvements in upper extremity function. Injections were well tolerated and safe. In

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Received for publication March 8, 2012; accepted in revised form December 12, 2012.

The authors would like to acknowledge the contributions of Kerry Dudziack, OT, and Melissa Steed, OT, for their assistance in evaluating study participants during the clinical trial.

L.A.K. and B.P.S. received funding as a prospective clinical grant from the Orthopaedic Research and Education Foundation (#97-035; $250,000; February 1997-January 2002). Allergan provided the vials of botulinum toxin type A (Botox; Allergan, Irvine, CA) necessary to complete this randomized, double-blind, placebo-controlled trial at no cost. All other expenses and salary support for all investigators was covered by research and development funds from the Department of Orthopaedic Surgery, Wake Forest School of Medicine, except for a gift of $60,000 from DT Scimed LLC (L.A.K. is a majority stockholder in this company). Funding from this gift was used to support biostatistical analysis of the study data. Allergan did not have a role in the design of the study, in the collection and interpretation of the data, in the writing of the manuscript, or in the decision to submit the manuscript for publication.

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0363-5023/13/38A03-0002$36.00/0
http://dx.doi.org/10.1016/j.jhsa.2012.12.019

contrast to other studies, study participants underwent multiple injection sessions based on their individual spasticity patterns. *(J Hand Surg 2013;38A:435–446. Copyright © 2013 by the American Society for Surgery of the Hand. All rights reserved.)*

Type of study/level of evidence Therapeutic I.

Key words Botulinum A toxin, cerebral palsy, double-blind, placebo-controlled trial, functional, outcomes, upper extremity.

Additional material is available online.

ALTHOUGH INJECTIONS of botulinum A toxin (BoNT-A) are used widely to manage spasticity in children with cerebral palsy, the use of toxin injections in the upper extremity continues to be evaluated. Children with cerebral palsy involving the upper extremity demonstrate characteristic spasticity patterns including shoulder internal rotation, elbow flexion, forearm pronation, wrist and finger flexion, and thumb-in palm. Prolonged muscle imbalance across upper extremity joints is associated with deleterious effects including increased dysfunction of agonist/antagonist muscles and exacerbation of nonspastic antagonist muscle weakness. These effects contribute to the development of muscle contractures, which, in turn, may lead to capsular tightness, flexion or extension contractures, and/or bony deformities. Children with upper extremity spasticity may have poor self-esteem and experience difficulties with functional activities.

A large percentage of children with cerebral palsy are not candidates for upper extremity surgery because of their age, the presence of fixed contractures or osseous deformities, and/or a concomitant diagnosis of movement disorders. There are incomplete data on the percentage of patients for whom soft tissue surgical procedures are effective. In addition, there are no published data to refute or contradict historical statements that only 10% to 20% of children with cerebral palsy are candidates for upper extremity surgery to improve function. The use of BoNT-A injections may provide an alternative treatment that balances forces across joints in a reversible and titratable manner. Theoretically, BoNT-A injections may increase the number of surgical candidates by decreasing the development of fixed contractures and osseous deformities prior to the age at which surgical timing is considered to be optimal.

Several randomized trials have demonstrated improved function, increased range of motion, decreased muscle tone, and improved appearance following upper extremity BoNT-A injections.[1–7] Although the chemodenervation produced by the toxin injections is reversible, several studies noted that the effects of BoNT-A injections appeared to improve function beyond the pharmacological effect of the toxin, which usually lasts from 60 to 90 days.[2,3] A randomized, double-blind, placebo-controlled trial included 14 patients who were followed up for 3 weeks following 1 toxin injection session.[1] Our study is a randomized, double-blind, placebo-controlled trial that includes a cross-section of children with cerebral palsy classified with mild, moderate, and severe involvement and dynamic deformities affecting the hand. In addition, the muscles injected were identified based on each child's spasticity pattern and included multiple injection sessions.

Our hypothesis was that intramuscular upper extremity BoNT-A injections improve upper extremity function. The specific aims of the study were to determine whether BoNT-A injections improved function and range of motion over a 26-week study period when muscle injection patterns were individualized based on each child's upper extremity spasticity pattern and to evaluate the safety of the injections.

METHOD

The institutional review board approved the study protocol, and the study protocol conformed to the ethical guidelines in the 1975 Declaration of Helsinki. The study was initiated in 1997, and study participant enrollment and follow-up were completed in February 2002. Parents/caregivers provided informed consent before their children were enrolled in the study. Children eligible for study participation were between 3 and 18 years of age with a diagnosis of hemiplegia, diplegia, or quadriplegia and dynamic upper extremity muscle imbalance interfering with physical functioning, limiting activities of daily living, causing discomfort, and/or compromising caregiver activities. At the time the trial began, there was no information regarding the age at which children might benefit from upper extremity BoNT-A injections. Therefore, the inclusion criteria included any children who were between 3 and 18 years of age if they did not have fixed upper extremity contractures. Exclusion criteria included previous upper extremity BoNT-A injections, fixed contractures, pre-