Original Research

The Effect of Neural Lesion Type on Botulinum Toxin Dosage: A Retrospective Chart Review

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Background: It is difficult to compare the dosage of botulinum toxin between different neurologic conditions because of the different methods of reported dosages. Botulinum toxin is used to manage spasticity in variety of neurologic conditions, and it is important for clinicians to know whether there are differences in the dosage injected on the basis of the etiology of spasticity.

Objective: To determine whether the type of neural lesion influences the dosage of botulinum toxin required to manage spasticity.

Design: Retrospective chart review.

Setting: Review of patients who visited an outpatient spasticity clinic.

Participants: We assessed medical charts from 99 patients with stroke, multiple sclerosis (MS), and cerebral palsy (CP) (n = 33 for each etiology). We collected information such as age, gender, weight, time of lesion, total dosage (per person, per limb, per muscle), injection location, and injections cycles.

Interventions: None.

Main Outcome Measurements: OnabotulinumtoxinA dose − total dose in one leg was calculated as a sum of the units of the toxin injected in all the leg muscles.

Results: Total dose of toxin injected was 161 ± 19 (mean ± standard error of mean) in patients with stroke, 175 ± 13 in patients with CP, and 225 ± 18 in patients with MS. The total dose in the legs (normalized to body weight; units/kg) was significantly different between the 3 groups (stroke, CP, MS; $P = .001$). Subsequent post-hoc tests revealed that total dose in the legs of patients with MS was significantly greater (88%) than patients with stroke ($P = .001$). Hip adductors and hamstrings were injected most commonly in MS and CP, but toe muscles were commonly injected in patients with stroke, whereas plantar flexors were evenly injected all 3 patient groups.

Conclusion: In our practice, we found that treating spasticity in people with MS required the greatest dose of botulinum toxin, followed by CP and then stroke.

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INTRODUCTION

Spasticity is a feature of upper motor neuron lesions seen in conditions such as stroke, multiple sclerosis (MS), and cerebral palsy (CP). Spasticity manifests as an increase in muscle tone characterized by a velocity-dependent increase in resistance to movement that often presents as debilitating stiffness, altered limb posture, and spasms. Treatments range from physical and occupational therapy to pharmacologic and surgical interventions. Among the pharmacologic interventions, botulinum toxin type A (BoNTA) injection therapy is used widely because it can be used to target treatment to specific muscles. BoNTA allows physicians to control the amount of injection required to induce desired clinical effects localized to the muscle injected. When injected into spastic muscles, this potent neurotoxin acts as a local muscle relaxant by blocking the release of acetylcholine from nerve terminals, thus inhibiting neuromuscular transmission. BoNTA has been used successfully to manage spasticity in patients with variety of underlying etiologies [1].

Although the etiologies of various neurologic conditions such as stroke, MS, and CP are different, they all may result in the clinical condition of spasticity. In adults, stroke usually

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results from hemorrhage or obstructed blood flow to the fully developed brain and is a static lesion that does not generally change over time. In those affected by MS, the demyelinating lesions may be localized in the brain, brainstem, cerebellum, spinal cord, of any combination of the aforementioned structures of the central nervous system. In contrast to stroke and MS, CP is a nonprogressive condition resulting from a neurologic injury to the developing brain occurring during the pre-, peri-, or postnatal period. Given such diverse conditions faced by patients with spasticity, toxin dosing must be driven by clear long-term functional goals against the backdrop of unique circumstances presented by spasticity originating from diverse etiologies.

Optimal dose (the least amount needed to reach a desired outcome without negative effect) can be influenced by numerous factors [2]. Factors such as severity, chronicity, and duration of spasticity, potential loss of residual function, as well as the number and type of muscles involved and the age and body mass of patients can influence dosage and can vary between patients and between etiologies. For example, although the impairments associated with CP are not progressive, the condition will not remain static as the child grows physically. Meanwhile, MS may be a progressive disorder, and the formation of new lesions results in a variable and dynamic spasticity profile [3]. In addition, data regarding total dosage in the arms and legs are limited to stroke and brain injury [4]. Thus, it is clinically important to document the dosage differences and patterns over time between patients with spasticity originating from various conditions to guide physicians regarding choice of dosage.

In very few studies do authors compare dosages across various neurologic conditions, and several challenges exist to efficiently understand these differences. Barnes et al [5] attempted to compare the dose of incobotulinumtoxinA in a variety of etiologies; however, their study had only 3 patients with MS and CP, whereas 87 patients with stroke were included. Another challenge in comparing dosage across etiologies is the heterogeneity of muscles or muscle groups injected in different patient groups. In addition, some studies do not separate the effects of botulinum toxin (BoNT) on different etiologies and instead group them together [6], making it difficult to differentiate the effects of etiologies on optimal dosage. Different dosage reporting conventions used in the literature also impose additional challenges in comparing dosage. A retrospective study of the medical charts of adult stroke, MS, and CP patients would provide a convenient way to examine the distribution of injections in various muscles in the arms and legs and the differences in botulinum dosage based on etiologies.

METHODS

The medical charts of patients who were treated with onabotulinumtoxinA (Allergan Inc., Irvine, CA) injections for upper or lower limb spasticity in our clinic from December 2008 to November 2011 were reviewed, and data regarding the treatment of patients with stroke, MS, and CP (33 patients per condition) were collected. This study was part of a larger study examining BoNTA dosage across 5 injections cycles. Thus, 99 patients who met this inclusion criterion were included in this chart review. We recorded age, gender, weight, time of lesion, total dosage from their first injection cycle (per person, per limb, per muscle), injection location, and injections cycles. Hip adductors, knee flexors (hamstrings group), plantar flexors (gastrocnemius, soleus, tibialis posterior), and toe muscles (extensor hallucis longus, flexor hallucis longus, flexor digitorum longus, and flexor digitorum brevis) were in injected in legs. Shoulder adductors (pectoralis major), elbow flexors (biceps brachii, brachilis, and brachioradialis), elbow extensors (triceps brachii), wrist flexors (flexor carpi radialis and flexor carpi ulnaris), long finger flexor (flexor digitorum profundus, flexor digitorum superficialis, flexor policis longus), and intrinsic hand muscles (interossii and thenar muscles) were injected in the arms.

Injections were delivered under the guidance of electromyography with electrical stimulation and in some cases under the guidance of ultrasound. Total dosage for legs and arms (ie, the sum of the units of the toxin injected in all muscles in the legs and in the arms) was calculated for all 3 patient groups. The amount of toxin injected per muscle was based on several factors: (1) the physician's perception of spasticity when typical clinical spasticity scales, such as the modified Ashworth scale and Tardieu scale, were used; (2) electromyographic signs of muscle overactivity; (3) range of motion and functional impairment because of spasticity; and (4) patient- and physician-identified clinical improvement goals. The physicians did not control or hold stable any other spasticity medications that our patients may have been taking. If they were on other neuroactive drugs, then it is possible that the dosage of such other drugs may have been changed on the basis of the degree of spasticity and related functional impairments. Both physicians who treated the current sample of patients are experts in BoNT injections with clinical experience with use of BoNT of greater than 10 years.

Data Analysis

A separate one-way analysis of variance (ANOVA) was used to compare the total leg dose and the total arm dose across 3 patient groups, and subsequent post-hoc paired t-tests were conducted to test between-group differences. The P value for ANOVA was set at .05, and a Bonferroni correction was used to recalculate the P value for paired t tests ($P = .017$). For between-group dosage comparison, dosage in the limb with greater number of muscles injected was used in patients with CP and MS. Thus, the limb with greater number of muscles injected in CP and MS groups was compared with the botulinum dosage on the paretic limb after stroke. Statistical tests were performed, and graphs