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Narrative Review

Botulinum Toxin Injection Techniques for the Management of Adult Spasticity

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Abstract

Spasticity is often experienced by individuals with injury or illness of the central nervous system from etiologies such as stroke, spinal cord injury, brain injury, multiple sclerosis, or other neurologic conditions. Although spasticity may provide benefits in some patients, it more often leads to complications negatively impacting the patient. Nonpharmacologic treatment options often do not provide long-term reduction of spasticity, and systemic interventions, such as oral medications, can have intolerable side effects. The use of botulinum neurotoxin injections is one option for management of focal spasticity. Several localization techniques are available to physicians that allow for identification of the selected target muscles. These methods include anatomic localization in isolation or in conjunction with electromyography guidance, electrical stimulation guidance, or ultrasound guidance. This article will focus on further description of each of these techniques in relation to the treatment of adult spasticity and will discuss the advantages and disadvantages of each technique, as well as review the literature comparing the techniques.

Introduction

Spasticity is one symptom often experienced by individuals with any injury or illness of the central nervous system and is classically described by Lance as "a motor disorder characterized by a velocity-dependent increase in tonic stretch reflexes (muscle tone) with exaggerated tendon jerks, resulting from hyperexcitability of the stretch reflex, as one component of the upper motor neuron syndrome" [1]. Although spasticity occasionally provides benefits in some patients, such as assisting with transfers or standing, it often leads to complications, including difficulty with hygiene, dressing, positioning, and the development of contractures and pain.

Botulinum neurotoxin (BoNT) injection is particularly effective as part of an overall treatment strategy to manage focal spasticity. Seven serotypes of BoNT exist; however, only the A and B (BoNT-A and BoNT-B) are used in clinical practice. AbobotulinumtoxinA (Dysport Ipsen Biopharm Ltd., Wrexham, UK; Medicis Pharmaceutical, Scottsdale, AZ), incobotulinumtoxinA (Xeomin; Merz Pharma, Frankfurt am Main, Germany), and onabotulinumtoxinA (Botox; Allergan, Inc., Irvine, CA) are the commercially available formulations of BoNT-A, and rimabotulinumtoxinB (MYOBLOC; Solstice Neurosciences, LLC, Louisville, KY) is the commercially available formulation of BoNT-B. Each of the serotypes exerts its effect by blocking the release of acetylcholine from the nerve terminal, thereby uncoupling the excitation-contraction process and weakening the injected muscle. To exert its effect, when injected into muscle, the BoNT is internalized into the nerve terminal and subsequently binds to a target protein involved in the process of exocytosis of the acetylcholine; this target protein is SNAP-25 for BoNT-A and VAMP/synaptobrevin for BoNT-B. By interfering with the docking of the acetylcholine vesicles at the nerve terminal, BoNT blocks acetylcholine release into the neuromuscular junction.

BoNTs were first introduced for clinical use in the 1980s for the treatment of strabismus. Since their introduction, BoNTs have been used for a variety of clinical conditions, including hypersecretory disorders, movement disorders, cosmetic applications, migraine treatment, as well as for use in the treatment of upper and lower limb spasticity. The clinical conditions for

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which these BoNT products have regulatory approval vary in different countries of the world. In the United States, approval from the Food and Drug Administration (FDA) for use in spasticity is limited to the use of onabotulinumtoxinA in the treatment of upper limb spasticity in adult patients. It is important to note that the FDA placed a boxed warning on all available toxins concerning risks of distant spread of toxin effect and implemented both the risk evaluation and mitigation strategy and the use of medication guides that describe the potential adverse effects. Furthermore, the FDA placed in the labeling of all available neurotoxins important language, noting that the potency units of these neurotoxins are specific to each preparation and assay method used, are not interchangeable, and that the units of potency of one neurotoxin cannot be compared or converted into units of another assessed with different assays.

Other treatment options exist beyond BoNTs for generalized spasticity; however, patients with very focal spasticity, intolerance to medication side effects, or insufficient spasticity management with these oral medications, including agents such as baclofen (Lioresal; Novartis Pharmaceuticals UK Ltd, Surrey, UK), dantrolene (Dantrium; JHP Pharmaceuticals, LLC, Parsippany, NJ), and tizanidine (Zanaflex; Acorda Therapeutics, Inc., Ardsley, NY), may obtain more optimal spasticity control with BoNT injections with fewer systemic effects than oral medications. When treating spasticity, the care team, including the physician, caregivers, and therapist, must determine appropriate treatment goals. Goals may include improvement in positioning, decreasing pain, and/or improvement in specific functional or passive care tasks such as hygiene or dressing.

Once treatment goals are identified, the physician is able to identify the most appropriate target muscles for treatment. There are several localization techniques available to physicians that allow for identification of the selected muscles. These methods include anatomic localization in isolation or in conjunction with electromyography (EMG) guidance, electrical stimulation (ES) guidance, or ultrasound (US) guidance. There are also other less frequently used localization techniques including fluoroscopy, computed tomography (CT), and endoscopic guidance. The goal of this article is to discuss the advantages and disadvantages of each injection technique and to review the literature in which authors compare the accuracy of muscle targeting and clinical outcomes on the basis of the injection technique used.

Methods

A literature search of PubMed and EMBASE databases was performed using the following search terms: botulinum toxin, neurotoxin, EMG, electromyography, electrical stimulation, motor point stimulation, ultrasound, ultrasonography, injection, targeting, accurate. This search returned 206 articles. The abstracts for each article were reviewed, and if the article did not compare different injection techniques, or evaluate clinical outcomes based upon the injection technique that was used, then the article was excluded. A total of 15 articles were included for discussion in this paper; 5 articles examined the accuracy of different injection techniques, and 8 articles described clinical outcomes resulting from injections performed with different injection techniques.

Techniques for Localization

The different techniques for localization will be discussed herein (Table 1). It is important to note that although certain methods for muscle localization may offer more precise targeting than others, the overall

Table 1
Injection techniques

Guidance	Requirements	Advantages	Disadvantages
Anatomical	No additional equipment required	Rapid	Unable to inject small or deep muscles Landmark dependent Limb position dependent Unexpected weakness from spread
EMG	EMG machine Monopolar needle	Accuracy of localization	Equipment cost Time Discomfort from needle adjustment
Electrical stimulation	Electrical stimulation machine Monopolar needle	Accuracy of localization	Equipment cost Time Discomfort from needle adjustment and stimulation
Ultrasound	Ultrasound machine	Visualization of target and surrounding muscles Accurate guidance with overlapping muscles Smaller needle and less pain compared with other guidance techniques	Equipment cost Requires significant practice

EMG = electromyography.