Needle Electromyography-Guided Chemodenervation

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In hypertonic disorders such as dystonia and spasticity, abnormal postures and reduced mobility impair functional movement. Selective denervation procedures attempt to improve integrated motor function by reducing abnormal postures and increasing range of motion. They may also reduce pain arising from sustained involuntary muscle contractions. Selective chemodenervation with intramuscular botulinum neurotoxin (BoNT) injections currently represents a primary treatment option in several hypertonic disorders including cranial, cervical, and limb dystonia; spasticity; hemifacial spasm; and motor tics. Due to the high quality of evidence-based information, recent evidence-based literature reviews recommend that BoNT be offered as a therapeutic option for cervical dystonia, adult spasticity, and childhood spasticity. Substantial evidence also supports offering BoNT as a treatment option to patients with blepharospasm, focal upper limb dystonia, adductor laryngeal dystonia, and upper limb essential tremor. Although supported by fewer controlled studies, BoNT should be a treatment consideration for patients with hemifacial spasm, focal lower limb dystonia, and motor tics.¹²

SELECTIVE DENERVATION

Selective surgical denervation procedures have been employed since the 19th century to treat cervical dystonia.³ Chemodenervation procedures with phenol and alcohol were later developed for treatment of spasticity and dystonia, though pain associated with their local chemical effects on tissue has limited enthusiasm for widespread use.⁴,⁵ The contemporary use of intramuscular BoNT for hypertonic disorders evolved from the work of Dr. Alan Scott to develop an alternative to strabismus surgery using BoNT injections into overactive extraocular muscles to produce temporary paresis. BoNT was subsequently employed to treat tonic activation of the orbicularis oculi muscles in blepharospasm and hemifacial spasm. After about 10 years of human treatment, BoNT A was licensed by the United States Food and Drug Administration (FDA) in 1989 for use in strabismus, blepharospasm, and hemifacial spasm. The FDA has subsequently approved use of specific formulations of BoNT A and B for cervical dystonia, and of BoNT A for upper limb spasticity and detrusor overactivity.
HYPERTONIC DISORDERS

Dystonia is defined by involuntary, sustained, patterned, and repetitive muscle contractions that generate abnormal postures with a tortional component. In spasticity, a velocity-dependent increase in muscle tone is associated with hyperactive tendon reflexes and features of the upper motor neuron syndrome.

Intramuscular BoNT injections may produce therapeutic effects by several mechanisms in dystonia and spasticity. Although the most apparent mechanism is reduced muscle contractile force due to neuromuscular blockade affecting extrafusal muscle fibers, modified sensory feedback may also be involved. BoNT paralyzes both extrafusal and intrafusal muscle fibers with reduced activation of muscle spindles and decreased afferent feedback to the central nervous system resulting in reduced α-motoneuron drive. In addition, BoNT may ameliorate pain by effects on sensory nociceptive systems.

BOTULINUM NEUROTOXINS

BoNTs are zinc endopeptidases that cleave a toxin-specific location of one or more of the SNARE (soluble N-ethylmaleimide-sensitive factor attachment protein receptor) proteins mediating the docking and fusion of acetylcholine vesicles with the presynaptic membrane at the neuromuscular junction, in autonomic ganglia, and in parasympathetic nerve terminals. SNARE proteins SNAP-25 (synaptosomal-associated protein of 25 kDa) and syntaxin are associated with the presynaptic membrane, while synaptobrevin or vesicle-associated membrane protein (VAMP) is located on the synaptic vesicle membrane. SNAP-25 is cleaved by types A, C, and E toxin, and syntaxin is cleaved by type C toxin. Synaptobrevin is cleaved by types B, D, F, G, and tetanus toxin. Following cleavage of SNARE proteins by BoNT, release of acetylcholine is permanently halted at affected synapses. Neuromuscular transmission is restored when the presynaptic neuron sprouts new nerve terminals to reform cholinergic synapses.

BoNT is thought to be the most toxic substance by weight, with a lethal dose in humans of approximately 1 ng/kg of type A toxin. The lethal dose of type A BoNT for a 70 kg man is estimated at 3000 units by intramuscular or intravenous routes based on primate data.

As a biological agent, BoNT is assayed and dispensed by bioactivity measured in mouse units. One unit of BoNT represents the lethal dose (LD₅₀) or the intraperitoneal dose required to kill half of the mice in a colony under defined conditions. Importantly, the dosing units of each proprietary type of BoNT are not interchangeable because of methodological differences in bioassay procedures. In order to minimize errors related to the increasing number of BoNT products and the unique dosing associated with each product, the FDA recently announced nonproprietary name changes for all BoNT products. The new nomenclature follows the World Health Organization guidelines for nonproprietary names in that they are “distinctive in sound and spelling and should not be liable to confusion with other names in common use.”

Commercial Botulinum Neurotoxin Preparations

Three commercial preparations of BoNT A are currently available. OnabotulinumtoxinA (Botox®, Allergan, Inc.) is supplied in 100 and 200 unit vials of lyophilized toxin and should be refrigerated at 2-8°C. The package insert recommends reconstitution of the lyophilized toxin with 0.9% sodium chloride without preservative. Concentrations of 100 units/mL and 50 units/mL are commonly prepared. Reconstituted toxin should be used within 4 hours at room temperature to ensure maximum potency. However, if refrigerated at 2-8°C, the reconstituted toxin can be used for up to 24 hours. AbobotulinumtoxinA (Dysport®, Ipsen Biopharm Ltd.) is supplied in 300 and 500 unit vials of lyophilized toxin. The vials should be protected from light and refrigerated at 2-8°C. The package insert recommends reconstitution of the lyophilized toxin with 0.9% sodium chloride without preservative to a concentration of 500 units/mL. Reconstituted toxin should be used within 4 hours to ensure maximum potency. IncobotulinumtoxinA (Xeomin®, Merz Pharmaceuticals GmbH) is the most recent BoNT to be approved for use by the FDA. It is supplied in 50 and 100 unit vials of lyophilized toxin, and packaged product may be stored at room temperature. The package insert recommends reconstitution of the lyophilized toxin with 0.9% sodium chloride without preservative. Concentrations of 100 units/mL and 50 units/mL are commonly prepared. Reconstituted toxin should be used within 4 hours at room temperature to ensure maximum potency. However, if refrigerated at 2-8°C, the reconstituted toxin can be used for up to 24 hours. RimabotulinumtoxinB (Myobloc®, Solstice Neurosciences, Inc.) is the only commercial preparation of BoNT B. It is supplied in 2,500, 5,000, and 10,000 unit vials of 5,000 unit/mL solution. Storage at 2-8°C is recommended, though undiluted rimabotulinumtoxinB is stable at room temperature for 9 months. If diluted with normal saline without preservative, the dilute toxin should be used within 4 hours.

Dosing Equivalence

Beyond the demonstrated dosing equivalence of onabotulinumtoxinA and incobotulinumtoxinA for
cervical dystonia, there is not a validated dosing ratio to facilitate changing between one BoNT and another. In order to provide some guidance for clinical practice, a discussion of approximate dosing ratios will follow. As noted from the experience in cervical dystonia cited above, the ratio of effect between onabotulinumtoxinA and incobotulinumtoxinA is about 1:1, and the ratio of therapeutic effect between abobotulinumtoxinA and onabotulinumtoxinA is about 3:1. The ratio between either of the BoNT A formulations and rimabotulinumtoxinB has not been determined and may not be a linear function. In a randomized, double-blinded comparison of onabotulinumtoxinA and rimabotulinumtoxinB in cervical dystonia, a ratio of 1 unit onabotulinumtoxinA toxin to 40 units rimabotulinumtoxinB toxin was used. The study found equivalent benefit of onabotulinumtoxinA and rimabotulinumtoxinB at 4 weeks following injection, though onabotulinumtoxinA had a somewhat longer duration of effect (onabotulinumtoxinA: 14 weeks, rimabotulinumtoxinB: 12.1 weeks).

Toxin Preparation

During BoNT preparation, factors that may inactivate the toxin should be avoided. Such factors include shaking or vigorously agitating toxin in solution, heating toxin beyond room temperature, aging abobotulinumtoxinA or onabotulinumtoxinA for more than 4 hours at room temperature, or allowing any BoNT to exceed room temperature. Injecting partially inactivated toxin or toxoid reduces the intended paralytic effect and increases a patient’s exposure to antigen and risk for developing resistance. Additional details regarding preparation and handling of BoNT are reviewed by Parish.

General Dosing Guidelines

The total BoNT dosage per injection session should be the absolute minimum necessary for clinical benefit to minimize side effects, risk for developing resistance, and cost. General factors that influence the dosage for individual muscles include muscle size, degree of electromyographic activation, and clinical response to previous BoNT injections in that muscle. If the muscle participates in more than one element of the movement or posture, a relatively higher toxin dose should be used. If the muscle participates in an element of the movement or posture, but counteracts another element, a relatively lower dose should be used.

Onset of weakness may begin within 48 hours, and maximal weakness usually develops in 5-14 days. The peak therapeutic effect lasts for about 12-16 weeks, but can be significantly longer in some patients. Repeat injections are usually necessary every 4-5 months.

NEEDLE ELECTROMYOGRAPHY-GUIDANCE FOR CHEMODENERVATION

Needle EMG guidance for chemodenervation may be used to improve accuracy, safety, and economy of toxin administration, particularly when affected muscles lie well below the skin surface or in close proximity to muscles not to be injected. Needle EMG assessment prior to chemodenervation may also help to plan toxin dosage and distribution by identifying hypertonic muscles, muscles with persistent neuromuscular blockade, and muscles with possible contracture. Needle EMG techniques that assist chemodenervation include: (1) needle EMG recordings with a monopolar injecting needle, (2) motor point stimulation procedures, and (3) diagnostic needle examination prior to injection of chemodenervation agents. Evidence supporting needle EMG-guided injections will be reviewed subsequently for applications in specific hypertonic disorders.

Recording With Injecting Needle

Needle EMG recordings may be monitored in real time using a monopolar injecting needle to record spontaneous motor unit potential activation corresponding to an abnormal movement. If there is no spontaneous abnormal movement during needle EMG recording as may occur in task-specific dystonia or spasticity, the subject can be asked to activate the targeted muscle, or the motor point of the targeted muscle may be electrically stimulated (see below). Such procedures verify that the tip of the injecting needle is located in the targeted muscle or targeted muscle fascicle. Toxin is subsequently administered from a syringe through the injecting needle into the muscle.

Motor Point Stimulation

Motor point stimulation techniques are sometimes employed in limb muscles in order to administer toxin precisely at the endplate zones when there is no spontaneous or voluntary activation. The monopolar injecting needle is positioned in the muscle belly and a small electrical stimulus (approximately 0.25-0.50 mA) is delivered. When the needle tip is at the endplate zone, a maximal muscle twitch is elicited with minimal stimulus intensity.

Diagnostic Needle Electrode Examination

A diagnostic needle electrode examination prior to BoNT injections identifies the hypertonic muscle or muscles and the relative degree of involvement when there are several potential muscles that may be responsible for an abnormal movement or posture.
Persistent neuromuscular blockade may also be identified by the diagnostic needle electrode examination, and this may be relevant when patients fail to respond to BoNT injections. The absence of neuromuscular blockade in a previously injected muscle suggests an insufficient toxin dose or possible immunological resistance to BoNT, while persistence of the abnormal posture despite electromyographic findings of neuromuscular blockade in an injected muscle may suggest that other muscles are responsible for the abnormal posture. Within 2 weeks of injection, needle EMG in muscles injected with BoNT should exhibit fibrillation potentials, positive sharp waves, and polyphasic, unstable motor unit potentials. Muscle contracture may be present when a muscle expected to participate in a posture exhibits no needle EMG activity when the posture is maintained (e.g., elbow flexion without needle EMG evidence for biceps brachii activation). Such muscles may also exhibit reduced insertional activity and increased resistance to needle movement related to fibrotic muscle changes. Chemodenervation in such a foreshortened muscle would be likely to render minimal benefit.

ULTRASOUND LOCALIZATION FOR CHEMODENERVATION

Musculoskeletal ultrasound guidance has been increasingly used to inject BoNT. This real time imaging modality can identify fascial borders to minimize direct spread of toxin and can help avoid complications from accidental puncture of nerves or arteries. By keeping the injectate within the targeted muscle, especially in the forearm where there are multiple adjacent muscles at varying depths, BoNT injections are more accurate at least when compared to surface anatomical landmarks. There is a learning curve to be proficient in this technique and specialized equipment is required.

MUSCLE SELECTION

Effective and safe chemodenervation requires identification of the appropriate hypertonic muscles for injection so that paralysis is selective for only the muscle or muscles participating in the abnormal movement or posture. Knowledge of anatomy and kinesiology is necessary to identify these hypertonic muscles. Following careful clinical observation of the abnormal movement and posture, a list of candidate muscles for injection is generated.

In blepharospasm, the identification process is very straightforward with the orbicularis oculi muscles solely responsible for involuntary forced eye closure. In limb dystonia, identification of candidate muscles is generally straightforward, but there are some movements that may be assisted by several muscles. For example, wrist flexion may owe to activation of the flexor carpi ulnaris, palmaris longus, and flexor carpi radialis muscles or various combinations thereof.

In cervical dystonia, identification of muscles involved in a particular neck posture or movement may prove difficult. This owes to the complex anatomy and physiology in the neck where 26 muscle pairs link the skull, cervical spine, upper thorax, and shoulder girdles. Many of these muscles serve redundant functions with regard to movement and posture, and the number of muscle activation patterns that may generate a given neck posture or movement is nearly limitless.

As noted above, in situations where there is uncertainty regarding which muscles are responsible for producing an abnormal movement or posture, a diagnostic needle EMG assessment prior to the intramuscular injection of BoNT may be helpful to identify the abnormally active muscles. This is particularly applicable in cervical dystonia in light of the complex anatomy and functional redundancy of muscles for neck movements.

INJECTION TECHNIQUE

BoNT injections should be performed at the end plate region in the muscle belly to maximize the paralytic effect. Motor unit action potentials with short rise time and without positive deflection are observed near the motor end plate. Muscle fascia retards the spread of BoNT by about 25%. Nevertheless, significant BoNT diffusion occurs from injection sites, and higher BoNT doses and volumes increase the degree of toxin spread. The repeated demonstration of increased neuromuscular jitter in muscles distant from those injected with BoNT confirms that BoNT injected in neck or facial muscles becomes systemically distributed.

ADVERSE EFFECTS

The most common, and often the most serious, side effect of BoNT injections is untoward paralysis from spread or regional diffusion of BoNT to nontargeted muscles. Specific complications relate to the anatomical region in which the BoNT is injected. For example, dysphagia is a common complication of BoNT injections in the neck for cervical dystonia, particularly with injections in the sternocleidomastoid muscles which lie in close proximity to the muscles of
TREATMENT FAILURES AND RESISTANCE

A lack of response may owe to incorrect muscle selection, inadequate toxin dose, inactivated toxin related to improper preparation or storage, or prior immunization against BoNT. Although a relatively low number of patients fail to exhibit any response to BoNT injections as primary nonresponders, about 10% of patients injected for cervical dystonia may develop resistance and become secondary nonresponders. Development of resistance should be avoided, as patients with dystonia and spasticity often have limited treatment options.

BoNTs are relatively large polypeptides with antigenic properties. As with any antigen, the inoculum size and exposure frequency are the most important variables associated with developing immunological and clinical resistance to BoNT injections. Loss of response to treatment with BoNT has been documented with injections exceeding 250 units of onabotulinumtoxinA, with a large cumulative toxin dose, and with injection intervals of shorter than 3 months. Therefore, BoNT injections should be performed no more frequently than every 3 months, and supplemental or “booster” injections should be avoided. The total BoNT dosage per injection session should be the absolute minimum necessary for clinical benefit.

In some secondary nonresponders, neutralizing antibodies to BoNT can be documented, while other patients with these antibodies continue to experience therapeutic responses to BoNT. BoNT neutralizing antibodies are not predictive of clinical resistance. Several functional tests are available to establish nonresponsiveness. Two of these involve visual inspection of muscle weakness at 1-2 weeks following injections of BoNT in the corrugator supercilii or frontalis muscles. Injections into the sternocleidomastoid and extensor digitorum brevis muscles at baseline with 2-week postinjection electrophysiologic assessments may assess the degree of induced neuromuscular blockade when there is a question of BoNT resistance. When resistance to one serotype of BoNT develops, treatment with another serotype may be effective.

SPECIFIC APPLICATIONS

Cervical Dystonia

BoNT injections represent the most effective available treatment in cervical dystonia. Controlled trials using BoNT A and B have demonstrated benefit in head posture and pain in at least 75% of patients. An evidence-based review identified seven well-designed, randomized, controlled (Class I) studies that support the use of BoNT in cervical dystonia, and it was recommended that BoNT be offered as a treatment option to patients with cervical dystonia (Level A recommendation). A safe and effective approach to treatment of cervical dystonia with BoNT requires a thorough knowledge of neck muscle anatomy and kinesiology to generate a list of candidate muscles for injection. Awareness of surrounding structures such as the jugular vein, brachial and cervical plexii, phrenic nerve, spinal accessory nerve, and carotid and vertebral arteries facilitates needle insertions and injections that avoid injury to these structures.

Assessment of postural deviation in cervical dystonia can be organized in terms of postural deviation in the axial plane (torticollis), in the coronal plane (laterocollis), and in the sagittal plane (anterocollis and retrocollis). Most patients with cervical dystonia have postural deviation in at least two of these planes. Sagittal and lateral shift and shoulder elevation are also important postural deviations to note. Patients are ideally assessed in a seated position. Cervical dystonia may completely resolve in a recumbent position, and it is difficult to assess and inject standing patients.

Knowledge of cervical spine anatomy and of the range of movements permitted by the cervical spine is important in order to begin to determine which muscles are dystonically active (Table 1).

Most lateral flexion and flexion/extension movements occur segmentally from C2 through C7. Long muscles spanning these segments are generally involved in lateral flexion and in flexion/extension. The majority
of head rotation occurs at the atlanto-axial joint, so that muscles acting across this joint (e.g., obliquus capitis inferior, splenius capitis, sternocleidomastoid) have mechanical advantage in eliciting head rotation. Functional groupings of neck muscles are listed in Tables 2, 3, 4, and 5.

Needle insertion sites and activation maneuvers for relevant muscles in cervical dystonia are listed below:

**Sternocleidomastoid**

Surface muscle contours are apparent in the anterolateral neck and are accentuated with contralateral head rotation against resistance. Activation occurs with contralateral head rotation against resistance.

**Splenius Capitis**

Needle electrode insertion is performed 3 cm below the mastoid process and 4-5 cm lateral to the midline. This site corresponds to the C3-C4 vertebral level where splenius capitis lies just deep to trapezius. Needle electrodes are inserted horizontally and perpendicular to the skin surface to a depth of approximately 2 cm. Activation occurs with ipsilateral head rotation against resistance.

**Longissimus Capitis**

Needle electrode insertion is performed 2 cm below the mastoid process at the posterior margin of the sternocleidomastoid. This site corresponds to the C2-C3 vertebral level where longissimus capitis lies just deep to the splenius capitis and posterior to the levator scapulae. Needle electrodes are inserted horizontally and perpendicular to the skin surface to a depth of 2.0-2.5 cm. Activation occurs with simultaneous ipsilateral rotation and lateral flexion against resistance. Due to the close proximity of the levator scapulae, if motor unit potentials are recorded with ipsilateral shoulder elevation, the needle electrode should be retracted and redirected more posteriorly.

**Scalenus Posterior**

The posterior triangle of the neck (bounded by sternocleidomastoid anteriorly, by the trapezius posteriorly, and by the clavicle inferiorly) is identified. At the C7-T1 vertebral level, the muscle fascicle situated most posteriorly in the triangle is palpated during deep inspiration and tentatively identified as the scalenus posterior. A needle electrode is introduced perpendicular to the skin and just subcutaneously at this site. During live recording, the needle electrode is advanced cautiously with the subject activating by inspiring deeply so that motor unit potential rise times are minimized. To prevent erroneous needle placement in levator scapulae, the subject also elevates the ipsilateral shoulder. If ipsilateral shoulder elevation results in motor unit firing, the needle electrode is removed and placed in the next anterior adjacent muscle fascicle, and the activation procedures are repeated.

**Scalenus Medius**

After the scalenus posterior is identified and evaluated, the scalenus medius is identified as the next anterior adjacent muscle fascicle in the posterior triangle at the C7-T1 vertebral level. Needle insertion and activation are otherwise similar to those for the scalenus posterior, except that shoulder elevation is deleted.

**Obliquus Capitis Inferior**

The C2 vertebral level is identified as a plane 2.5 cm below the mastoid process (3.0 cm below the occipital bone). The needle electrode is introduced at this level midway between the posterior border of the sternocleidomastoid and the dorsal midline. With live recording, the needle electrode is advanced and directed somewhat cranio-medially toward the posterior arch of the atlas to a depth of 3.0-3.5 cm. During needle electrode advancement, the subject activates with gentle ipsilateral rotation against resistance. The needle electrode is advanced through the splenius capitis and no further than necessary to minimize motor unit potential rise time.

**Levator Scapulae**

The medial angle of the scapula is identified by palpation. Needle electrode insertion is performed at 3-4 cm cephalad and 1-2 cm medial to the medial angle of the scapula. This site corresponds to the T1 vertebral level where levator scapulae lies just deep to

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<table>
<thead>
<tr>
<th>Table 1. Movements permitted by the cervical spine (after Jofe)</th>
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<tbody>
<tr>
<td><strong>Occipital bone-C1</strong></td>
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<tr>
<td>----------------------</td>
</tr>
<tr>
<td>C1-C2</td>
</tr>
<tr>
<td>C2-C7</td>
</tr>
</tbody>
</table>
trapezius. Needle electrodes are inserted perpendicular to the skin surface to a depth of approximately 2.5 cm. A mild degree of ipsilateral scapular elevation is used for activation.

**Rectus Capitis Posterior Major**

The needle insertion site at the C1-C2 level is 1 cm below the occipital bone and 2 cm lateral to the midline. After the needle electrode is introduced at this site, it is directed through the semispinalis capitis toward the posterior arch of the atlas. Activation with head extension against gentle resistance is performed as the electrode is advanced. With live recording, the needle electrode is advanced no further than necessary to minimize motor unit potential rise time, which corresponds to a depth of 2.5-3.5 cm.

Cervical dystonia is characterized by involuntary, dystonic posturing of the neck and head and is produced by numerous neck muscles acting together or in isolation in complicated and abnormal activation patterns. In addition, the normal reciprocal inhibition between agonist and antagonist muscles is disordered, and there may be inappropriate inhibition of muscles that should oppose the abnormal movement. Some muscles exhibit arrhythmic bursts of activity that correspond with jerking head movements or a rhythmic firing pattern with head tremor. By contrast, in seated normal control subjects, virtually no needle EMG activity is found in most neck muscles with less than 20 degrees deviation from neutral head positioning. Needle EMG assessment of muscle activation is helpful to determine which candidate muscles based upon a
clinical assessment of the abnormal neck posture or movement are most responsible for the abnormal movement and posture.

In assessing such patients, consideration must be given to the postural dynamics and how an alteration of the strength of the involved muscles may affect each component of the abnormal posture. For example, if a patient has both head rotation (torticollis) and neck extension (retrocollis), weakening of the contralateral sternocleidomastoid may increase the degree of neck extension. Thus, it may be wiser to selectively weaken other muscles that rotate the head that do not flex the neck. Unfortunately, there is no prescribed formula for predetermining which muscles are involved in a given head posture, and treatment must be individualized for every patient. Most patients respond well to total doses of 100-250 units of onabotulinumtoxinA or incobotulinumtoxinA, 250-1000 units of abobotulinumtoxinA, or about 5,000-10,000 units of rimabotulinumtoxinB. Toxin dosing guidelines for individual neck muscles using needle EMG-guided injections are listed in Table 6.

The most characteristic abnormality is motor unit potential firing that directly correlates with movement as the head assumes the abnormal posture without voluntary attempts to oppose the movement. There is often continuous activation of the muscle with complete loss of reciprocal inhibition. With voluntary attempts to resist the abnormal posture, there may be a partial loss of reciprocal inhibition initially, followed by gradually increasing recruitment of motor unit potentials accompanied by the patient’s failure to maintain the position opposing the abnormal posture. There is often some loss of ability to activate muscles that should oppose the abnormal movement. A superimposed, irregular, bursting firing pattern is often seen and corresponds with a visible head tremor that is somewhat irregular and multiplanar.

In the absence of needle EMG-guidance, needle placement in dystonic neck muscles is often inaccurate. In one study in which needles were placed in neck muscles using clinical examination and surface landmarks without needle EMG guidance, the superficially-located sternocleidomastoid muscle was missed on 17% of needle insertions, and the levator scapulae was missed on 53% of needle insertions. Several studies in cervical dystonia have demonstrated an improved ability of needle EMG to identify dystonic muscles for injection, and to deliver toxin more accurately to dystonic muscles. In a blinded study of cervical dystonia assessing response with and without needle EMG assistance, an increased degree of improvement and a larger number of patients with marked improvement was observed when dystonic muscles were identified and injected under needle EMG guidance compared to patients receiving clinical assessment without needle EMG assistance.

Adverse effects of BoNT injections for cervical dystonia relate mainly to local toxin diffusion and include dysphagia, neck extensor weakness with “dropped head” syndrome, hoarseness, and dry mouth. Dysphagia is a particular issue with injections in the sternocleidomastoid muscle, and toxin dosages should therefore be minimized in anterior neck muscles. In one series, one-third of patients developed new symptoms of dysphagia following neck muscle injections for cervical dystonia. Dysphagia may be severe, and three patients required feeding tubes for up to 2 months due to dysphagia in one series. Patients that experience dysphagia due to oropharyngeal paresis are at risk for aspiration and for potential airway occlusion in extreme cases.

**Blepharospasm and Hemifacial Spasm**

In blepharospasm, dystonic contraction of the upper facial and orbicularis oculi muscles may produce eye irritability and blinking in mild disease with forceful, sustained eye closure in advanced disease. Therapeutic options in blepharospasm were limited.

<table>
<thead>
<tr>
<th>Muscle</th>
<th>OnabotulinumtoxinA (units)</th>
<th>IncobotulinumtoxinA (units)</th>
<th>AbobotulinumtoxinA (units)</th>
<th>RimabotulinumtoxinB (units)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sternocleidomastoid</td>
<td>5-60</td>
<td>15-180</td>
<td>15-90</td>
<td>250-1500</td>
</tr>
<tr>
<td>Scalene</td>
<td>5-30</td>
<td>15-90</td>
<td>125-750</td>
<td></td>
</tr>
<tr>
<td>Splenius capitis/cervicis</td>
<td>10-80</td>
<td>30-240</td>
<td>250-2500</td>
<td></td>
</tr>
<tr>
<td>Levator scapulae</td>
<td>5-60</td>
<td>15-240</td>
<td>250-2500</td>
<td></td>
</tr>
<tr>
<td>Longissimus capitis</td>
<td>10-80</td>
<td>30-240</td>
<td>250-2500</td>
<td></td>
</tr>
<tr>
<td>Semispinalis capitis</td>
<td>10-80</td>
<td>30-240</td>
<td>250-2500</td>
<td></td>
</tr>
<tr>
<td>Obliquus capitis inferior</td>
<td>5-50</td>
<td>15-150</td>
<td>250-1250</td>
<td></td>
</tr>
<tr>
<td>Rectus capitis posterior major</td>
<td>5-50</td>
<td>15-150</td>
<td>250-1250</td>
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</table>
prior to the introduction of BoNT injections, as oral medications are effective only in about half of these patients.\textsuperscript{75}

BoNT injections have demonstrated their effectiveness in treating blepharospasm in open studies and controlled trials,\textsuperscript{76} with durable improvement in longitudinal studies.\textsuperscript{77} An evidence-based review of BoNT in blepharospasm cited two well-designed Class II studies with probable effect and minimal side effects, and recommended that BoNT be considered as a treatment option in blepharospasm (Level B recommendation).\textsuperscript{1} In hemifacial spasm, BoNT injections dramatically improve the frequent, repetitive, unilateral paroxysmal contractions of facial muscles.\textsuperscript{78} Owing to the paucity of controlled clinical trials of BoNT in hemifacial spasm, an evidence-based review concluded that BoNT may be considered for treatment (Level C recommendation).\textsuperscript{1}

The techniques used for performing injections in blepharospasm and hemifacial spasm are similar, except that hemifacial spasm injections are unilateral, and somewhat lower doses of BoNT are used. Injections are distributed in the orbicularis oculi muscle using very low dosages per muscle (e.g., 8-30 units of onabotulinumtoxinA). The sites in the orbicularis oculi commonly injected include the superomedial aspect of the muscle near the corrugator supercilii and procerus, and in the lateral and inferior regions of the muscle. BoNT injected in the inferior aspect of the muscle diffuses into the lower facial muscles and usually obviates the need to perform separate injections in lower facial muscles in patients with blepharospasm and lower facial dystonia or in patients with hemifacial spasm and prominent lower facial synkinetic movements.

Injections in the midportion of the superior aspect of the muscle near the tarsal plate are to be avoided, as this may cause ptosis due to diffusion of toxin into the levator palpebrae muscle. Injections in the lower medial aspect of the lid should also be avoided to prevent diplopia related to diffusion of toxin into the inferior oblique muscle. In addition to ptosis and diplopia, adverse effects include eye dryness with corneal exposure keratitis related to excessive paralysis of the orbicularis oculi and periorbital ecchymosis related to needle injury of facial veins.

**Limb Dystonia**

In brachial dystonia or writer’s cramp, BoNT injections are effective in improving function and in reducing pain related to sustained muscle contractions.\textsuperscript{79} The American Academy of Neurology evidence-based review of BoNT in limb dystonia concluded that BoNT is probably effective (Level B recommendation) for treatment of focal upper limb dystonia based on several trials including one well-designed randomized (Class I) trial.\textsuperscript{80} Although the results of one Class II study suggested that BoNT may be effective for focal lower limb dystonia,\textsuperscript{81} there was not deemed to be enough data to make a treatment recommendation.

Brachial dystonia is most commonly focal and task-specific. It involves upper extremity muscle contractions and abnormal postures elicited by movements that are highly-controlled and repetitive, such as handwriting, typing, playing a musical instrument, golfing, or other occupational activities involving highly-controlled repetitive movements. The dystonia is elicited by and interferes with a limited set of tasks with otherwise normal motor function for other activities using the same muscles.

Clinical observation at rest and during performance of the inciting task is essential to muscle selection for chemodenervation. Unlike the neck where functional redundancy allows several muscles to generate a movement or posture, there is little functional redundancy in antebrachial muscles. Therefore, excessive BoNT dosing in a single muscle may significantly paralyze the wrist and hand with significant functional consequences. BoNT dosing should therefore be conservative, particularly in the finger extensors (Table 7).

Accurate injection needle placement in the intended muscle or muscle fascicle is essential in limb dystonia, and needle EMG-guidance permits proper muscle and muscle fascicle localization. One study assessed needle electrode placement in brachial dystonia in the absence of needle EMG.\textsuperscript{82} Experienced injectors reached the target muscle in only 37% of placement attempts, an unintended muscle was reached in 47% of placement attempts, and 16% of placement attempts were outside of any muscle. Patients should understand that BoNT injections for brachial dystonia sacrifice strength for the sake of potentially improved motor control for a specific task or group of tasks. BoNT doses are significantly higher in the lower limb (Table 8).

**Spasticity**

Disability related to reduced functional limb use and pain related to tonic muscle contractions may occur in spasticity. BoNT injections have elicited significant reductions in muscle tone in spastic upper limbs in controlled studies. In a multi-center trial using onabotulinumtoxinA in upper limb spasticity, wrist and finger flexor tone and disability were significantly
reduced in about two-thirds of patients. An American Academy of Neurology evidence-based review of BoNT treatment of spasticity cited 14 adult and six pediatric spasticity studies and concluded that BoNT should be offered as a treatment option (Level A recommendation) in these patients.

By comparison with limb dystonias, relatively higher doses of BoNT are required.

In the upper limb, spastic postures may include shoulder internal rotation and adduction, elbow flexion, forearm pronation, wrist flexion, finger flexion, and thumb flexion in the palm. In the lower limb, spastic postures include hip flexion, hip adduction, knee extension or flexion, equinovarus or valgus foot posturing, and great toe extension (striatal toe).

### SUMMARY

Accumulating clinical experience and experimental evidence demonstrates the value of selective chemodenervation with BoNT as an important primary mode of treatment for an increasing number of hypertonic disorders. Needle EMG guidance for chemodenervation, particularly for injection of deep cervical muscles and brachial muscles, may help to optimize the effectiveness and safety of these procedures.

### REFERENCES


<table>
<thead>
<tr>
<th>Table 7. Typical doses of botulinum toxin in brachial dystonia using needle electromyography-guided injections</th>
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</thead>
<tbody>
<tr>
<td><strong>OnabotulinumtoxinA, IncobotulinumtoxinA</strong></td>
</tr>
<tr>
<td>Muscle (units)</td>
</tr>
<tr>
<td>Flexor carpi ulnaris</td>
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<td>Flexor carpi radialis</td>
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<td>Flexor pollicis longus</td>
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<th>Table 8. Typical doses of botulinum toxin in lower limb dystonia using needle electromyography-guided injections</th>
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<tr>
<td><strong>OnabotulinumtoxinA, IncobotulinumtoxinA</strong></td>
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<td>Tibialis posterior</td>
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<tr>
<td>Flexor hallucis longus</td>
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<tr>
<td>Extensor hallucis longus</td>
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</tbody>
</table>
27. Albanese A. Terminology for preparations of botulinum neurotoxins: what a difference a name makes. JAMA 2011;305:89-90.
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