Introduction

Botulinum neurotoxin (BoNT) has proved to be a remarkably effective therapy for numerous movement disorders associated with muscle overactivity such as dystonia and related disorders, as well as spasticity [Table 1]. Additional therapeutic benefits accrue from actions such as blockade of acetylcholine release at autonomic nerve analysis as well as the blockade of release of nonacetylcholine transmitters at peripheral nerve endings.

Three broad categories of undesirable side effects are seen with BoNT. These are[1] diffusion of toxin into neighboring muscles and nerve endings,[2] sustained neuro-transmission blockade producing effects akin to anatomic denervation, and[3] development of antibodies to BoNT with subsequent immuno-resistance.[1]

Indications

Most appropriate conversion factor between Botox and Dysport units is less than 3 in cervical dystonia.[7]

Relative Contraindications

These include any excessive weakness, fixed contractures and neuromuscular disease such myasthenia gravis, Eaton-Lambert syndrome, and motor neuron disease. Other relative contraindications include pregnancy and lactation and the concurrent use of aminoglycosides.

Assessment

This would include a detailed clinical examination and a video analysis for later comparative evaluation. Patient education and counseling are essential and treatment goals should be agreed and documented. Consent should be obtained and BoNT should be prescribed. Secondary causes of treatable dystonia such as drugs or Wilson's disease should be ruled out. Physicians administering BTX should have a good understanding of both the anatomy of affected muscles and the resultant movement disorder. EMG monitoring helps diagnose the underlying disorder and identify appropriate muscles for injection.

Goals for Treatment

Dystonia

Treatment of focal dystonia with BoNT is designed to improve the patients’ postures and function and to relieve associated pain. BoNT temporarily weakens dystonic muscles, thereby allowing more normal posture and function. The benefits that BONT conveys to a particular patient depend on the localization and relative degree of severity of the dystonic muscles being injected. The decision to combine injections of BTX-A with other forms of treatment for dystonia is based on associated factors and individual decision.

Blepharospasm

Blepharospasm may be idiopathic or induced by drugs such l-dopa or neuroleptics. It needs to be differentiated from facials in patients with Tourette's syndrome and apraxia of eyelid opening.

The injections are done on an outpatient basis. Intradermal injection with a 27–30-gauge needle is recommended. Typically 3–5 points around each eye are injected. The principle is to avoid the midportion of the upper eyelid to avoid inadvertent diffusion into the levator palpebrae superiors, which would lead to undesirable ptosis.

Focal hand dystonia

Among these, Writer’s cramp is the most common form of occupational dystonia. However, these has been described in those professional whose work involves frequent and repetitive movements such as musicians, typists, milkers, cashiers,
Table 1: Dosage of botulinum toxin for various indications

| Indication                          | Dosage                        | References |
|-------------------------------------|-------------------------------|------------|
| Dystonia                            |                               |            |
| Blepharospasm                       | 12.5–25 units/eye Botox       | [2-6]      |
| Cervical dystonia (Torticollis)     | 50–90 units/eye Dysport       | [5]        |
| Oromandibular – facial – lingual dystonia masseters and temporalis | Up to 50 units Botox in each muscle | [15]      |
| Spasmodic dysphonia                 |                               |            |
| Adductor                            | 15 unilat or 2.5–5 units bilat/TA | [16-20] |
| Abductor                            | 3.75 units/PCA (unilat) serially | [21]      |
| Focal limb dystonia (including Writer’s cramp) | Individualized dosages | [22-28] |
| Hemifacial spasm                    | 17.5 units Botox               | [9]        |
| Dystonic tics                       | 70 units Dysport               | [9]        |
| Oromandibular – facial – lingual dystonia masseters and temporalis | Individualized dosages | [15]      |
| Spasmodic dysphonia                 |                               |            |
| Adductor                            |                               | [21]      |
| Abductor                            |                               | [20]      |
| Focal limb dystonia (including Writer’s cramp) | Individualized dosages | [22-28] |
| Cervical dystonia (Torticollis)     | 60–374 units Botox             | [7-9]      |
| Oromandibular – facial – lingual dystonia masseters and temporalis | Up to 50 units Botox in each muscle | [15]      |
| Spasmodic dysphonia                 |                               |            |
| Adductor                            | 15 unilat or 2.5–5 units bilat/TA | [16-20] |
| Abductor                            | 3.75 units/PCA (unilat) serially | [21]      |
| Focal limb dystonia (including Writer’s cramp) | Individualized dosages | [22-28] |
| Hemifacial spasm                    | 17.5 units Botox               | [9]        |
| Dystonic tics                       | 70 units Dysport               | [9]        |
| Oromandibular – facial – lingual dystonia masseters and temporalis | Individualized dosages | [15]      |
| Spasmodic dysphonia                 |                               |            |
| Adductor                            |                               | [21]      |
| Abductor                            |                               | [20]      |
| Focal limb dystonia (including Writer’s cramp) | Individualized dosages | [22-28] |
| Cervical dystonia (Torticollis)     | 125–1200 units Dysport         | [9-11]     |
| Oromandibular – facial – lingual dystonia masseters and temporalis | Up to 50 units Botox in each muscle | [15]      |
| Spasmodic dysphonia                 |                               |            |
| Adductor                            |                               | [21]      |
| Abductor                            |                               | [20]      |
| Focal limb dystonia (including Writer’s cramp) | Individualized dosages | [22-28] |
| Hemifacial spasm                    | 17.5 units Botox               | [9]        |
| Dystonic tics                       | 70 units Dysport               | [9]        |
| Oromandibular – facial – lingual dystonia masseters and temporalis | Individualized dosages | [15]      |
| Spasmodic dysphonia                 |                               |            |
| Adductor                            |                               | [21]      |
| Abductor                            |                               | [20]      |
| Focal limb dystonia (including Writer’s cramp) | Individualized dosages | [22-28] |
| Cervical dystonia (Torticollis)     | 579–19853 units Myobloc        | [9], [12-14] |
| Oromandibular – facial – lingual dystonia masseters and temporalis | Up to 50 units Botox in each muscle | [15]      |
| Spasmodic dysphonia                 |                               |            |
| Adductor                            |                               | [21]      |
| Abductor                            |                               | [20]      |
| Focal limb dystonia (including Writer’s cramp) | Individualized dosages | [22-28] |

Cervical Dystonia

The movements of the neck – rotation, anterior, and posterior flexion, tilt, and shift in the antero–posterior or lateral planes – can occur in any combination in cervical dystonia. This can be associated with shoulder involvement as well as jerky or tremulous movements and also pain. Muscles involved in the abnormal posturing are isolated using standard anatomic landmarks. The most commonly injected muscles include sternocleidomastoid, trapezius, splenius capitis, levator scapulae, and scalene complex. Usually 2–6 muscles are injected at muscle sites. The BTX should be injected along the belly of the muscle to allow for adequate diffusion. Comella et al.\(^{[33]}\) reported a significantly greater magnitude of improvement in those cases where the treated neck muscles were selected by clinical and electromyographic guidance than the cases in which only clinical examination was used.

Oromandibular dystonia

This typically involves the masticatory, lower facial, and tongue muscles and is associated with jaw deviation and spasm. BTX should be injected into the inappropriately contracting muscles in different combinations including masseter, temporalis lateral pterygoids, and submental muscles. The lingual muscles need to be injected carefully.

Laryngeal dystonia

They are three types—adductor spasmodic dysphonia (strained strangled voice), abductor spasmodic dysphonia (whispering voice), and adductor breathing dysphonia (paradoxical vocal fold motion). The thyroaarytenoid muscles are located with EMG guidance, and percutaneous injections of BTX are administered through the cricothyroid membrane. Bilateral injection approach is the most common technique for adductor dysphonia, while for the rarer abductor variety unilateral injections are done serially into the posterior cricoarytenoid muscles.

Hemifacial spasm

This can be a very disabling disease because severely affected individuals are socially handicapped and functionally blind. This can involve any combination of orbicularis oculi, frontalis, risorius, zygomaticus major, and platysma muscles. Injections of BTX are given according to the muscles in spasm which differ from patient to patient.

Palatal Tremor (myoclonus)

This may be idiopathic or symptomatic. BTX injection of the tensor veli palatini muscle may reduce the symptom by reducing the amplitude of myoclonic jerk.

Bruxism

This is an involuntary chewing such as rhythmic jaw movement occurring especially at night, with grinding of the teeth. In this disease, BoNT is injected into the most sore part of the muscle, weakening the most spastic part of the masseter muscle without affecting the ability to chew.

Tics

These can be either motor or phonic tics. Both of these can be simple or complex and also classified as clonic, tonic, and dystonic. BoNT produces significant decrease in both tic frequency and urge to tic. It improves the quality of life as reported by the patients. One has to be cautious of producing hypophonia.

Outcome measurement and follow up

Measurement methods include the use of physical measures, techniques to quantify individual symptoms or benefits, such
as visual analogs scales and verbal scales as well as other rating scales. Follow-up appointment should be at approximately 3–17 weeks post injection using the same assessment as pre injection. It should be assessed again 4–6 months interval.

Spasticity
Symptomatic improvement decreases spasm frequency and relief of pain. There is a reduction of generalized spasticity – it facilitates sitting, and positioning or standing and also allows wearing of orthosis. In functional improvement it improves mobility in terms of speed, quality or endurance of gait, endurance of wheel chair propulsion, improves ease and safety of transfers, dexterity and reaching. There is decrease in burden on care givers such as positioning (e.g., feeding) care and hygiene, e.g., washing and catheterization, dressing, decreases care time to allow quality time. In prevention of complications, it prevents unnecessary use of antispasmodic and others medications, and also prevents pressure sores and contractures. It prevents or delays surgery. Cosmetically, it improves body image.

BoNT injection
BoNT should be offered as a treatment option to reduce muscle tone and improve passive function in adults with spasticity (Level A) and should be considered to improve function (Level B). Patient should be selected for BoNT depending on the focal spasticity, dynamic spastic component, clearly identified goals for treatment and anticipated functional gains. Patient and their families/care givers should be given adequate information, prior to treatment and should agree goals before treatment is given. Informed consent should be obtained from patients prior to injection. If the patient does not have the mental capacity to concern current policies for obtaining consent should be followed. The maximum dose used in a single treatment should not exceed 1500 mu Dysport (Ipsen), 400 U Botox (Allergan) or 10,000 U Myobloc. The dose of BoNT should be injected intramuscularly depends on the muscle size. Small muscles such as the open cords receive 0.75 U, whereas larger neck muscles may require 100–150 U and lower limb muscles may require 200–300 U to exert a desirable effect.

Other services
BoNT injection must be a part of rehabilitation program involving postinjection exercise, muscle stretch and/splinting, to achieve an optimal beneficial clinical effect. Clinical should have access to facilities to aid in assessment, selection and treatment planning, e.g., electromyography (EMG). Clinical should familiarize themselves with a single agent to avoid confusion over dose.

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