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1. Introduction

Dystonia and Spasticity, both clinically manifesting with muscle hyperactivity, are symptomatic targets for Botulinum toxin (mainly type A, and referred to here as BoNT) injection. Certain differences exist in their phenomenology and complexity, hence the need to highlight those intricacies, as relevant in the clinics. This introductory chapter therefore aims to provide a framework upon which the practical applications of BoNT in dystonia and spasticity may be applied in contemporary times. The other chapters in this book will likewise discuss aspects of BoNT from the basic to the clinical side, including the current use of instrument-guided injections and tandem neuro-rehabilitation.

2. Dystonia Phenomenology

The contemporary definition and phenomenology of dystonia, bears the following key points, as derived from Movement Disorders Society:

(1) “Dystonia is a movement disorder characterized by sustained or intermittent muscle contractions causing abnormal, often repetitive, movements, postures, or both. Dystonic movements are typically patterned, twisting, and may be tremulous. Dystonia is often initiated or worsened by voluntary action and associated with overflow muscle activation.”

(2) Phenomenology of dystonia includes influence of voluntary action, tremor occurrence, motor overflow and mirror movements.

(3) Alleviating maneuvers to reduce or abolish dystonia.
A Multi-axial diagnostic approach for dystonia includes the following:

1. **Axis I (Clinical characteristics):** Age of onset, body distribution, temporal pattern and associated features.

2. **Axis II (Etiology):** Nervous system pathology, inherited, acquired or idiopathic.

3. **Treatment of dystonia range from oral medications, chemodenervation (with BoNT and muscle afferent block), neurorehabilitation and functional surgery.**

### 3. Botulinum Toxin for Dystonia

BoNT, as applied in dystonia is well established for focal, segmental and task-specific dystonias. The advantage of BoNT in dystonia is hinged on the following: (1) Dual mechanistic effects of BoNT along extrafusal (hence in muscle hyperactivity) and intrafusal (hence in posturing and muscle afferent modulatory effects along spinal and supraspinal networks) muscles; (2) Targeted therapy in focal muscular spasms; (3) Aims that improve quality of life and functioning; (4) “Tailored fit” based on the variable dystonic patterns; and (5) Repeated but robust and safe injections over time. In fact, BoNT may be considered as a “sensory trick” acting via proprioceptors, that not only alleviate muscle spasms at injected, but also contiguous areas in overflow. The usual aims of BoNT in dystonia range from relief of spasms, improve posture, pain reduction, cosmesis, and prevention of contractures, bone and joint instability, dislocation and occurrence of radiculopathy. BoNT may still have roles in generalized dystonias, where

<table>
<thead>
<tr>
<th>Dystonia severity</th>
<th>Dystonia localisation</th>
<th>Primary treatment</th>
<th>Additional treatment</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>Focal</td>
<td>ADD/none</td>
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<td></td>
<td>Widespread</td>
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<tr>
<td>Moderate</td>
<td>Focal</td>
<td>BTT</td>
<td>RT (optional)</td>
<td>In antecollis and alternating torticollis consider DBS</td>
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<td>Widespread</td>
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</tr>
<tr>
<td>Severe</td>
<td>Focal</td>
<td>BTT</td>
<td>RT ADD (optional) AD (optional)</td>
<td>In case of insufficient effect consider DBS</td>
</tr>
<tr>
<td></td>
<td>Widespread</td>
<td>BTT</td>
<td>RT ADD (optional) AD (optional)</td>
<td>Either test BTT first or recommend DBS straight away</td>
</tr>
<tr>
<td></td>
<td>DBS</td>
<td>RT BTT</td>
<td>ADD (optional) AD (optional)</td>
<td></td>
</tr>
</tbody>
</table>

AD, adjuvant drugs; ADD, antidystonic drugs; BTT, botulinum toxin therapy; DBS, deep brain stimulation; RT, rehabilitation therapy; physiotherapy, re-training, occupational therapy, speech therapy, sociotherapy, psychotherapy, patients groups.

**Table 1.** Algorithm for treatment of dystonia.
specific aims are geared to improve quality of life and functioning. An example will be BoNT for oro-mandibulo-lingual dystonias aimed at feeding and nutrition. In addition, BoNT in dystonia may still be combined with onboard oral medications and even following functional neurosurgery.

Neurological Practice Guidelines forwarded by the American Academy and European Federation indicated Level A Recommendation for BoNT in Focal dystonias, especially blepharospasm, cervical dystonia and writer’s cramp. Likewise, recommendations based on dystonia severity, applying a number of management strategies, have been recently published by the IAB—Interdisciplinary Working Group for Movement Disorders Special Task Force on Interdisciplinary Treatment of Dystonia (Table 1 from Dressler et al, Journal of Neural Transmission, 2015, with permission).

4. Spasticity and its Complexity

Spasticity may complicate stroke, multiple sclerosis (MS), cerebral palsy (CP), traumatic brain injury (TBI), spinal cord injury, hereditary spastic paraplegia as well as retroviral and other infectious spinal cord disorders.

Spasticity, as it arises from the involuntary activation of muscles, whether intermittent or continuous, may lead to pain, disability, functional impairment and eventually contractures. In the case of stroke, about a third of survivors have significant post-stroke spasticity (PSS) and among those presenting in the hospital, about half develop at least one severe contracture. Being a complex condition, spastic paresis substantially impacts on patients’ and caregivers’ quality of life. Hence, spasticity management may engage interdisciplinary sub-specialties. To date, the varied rehabilitation practices in spasticity are generally aimed at prevention of secondary complications, minimizing aggravating factors, perhaps losing focus on the abnormal muscle activity itself. For instance, it is now understood that the critical factor in movement impairment in spastic paresis is the overall involvement of antagonist resistance, whether of a reflex nature or not. In addition, a wider problem area in spasticity is the fact that management should also address spasticity-related co-contraction, dystonia, associated reactions, local biomechanical changes and contracture. This present work aims to show how, incorporating BoNT injection in neurorehabilitation practices, could pave the available treatment avenues toward improving, not only muscle tone, but also other related disabilities of the paretic limb afflicted with spasticity. Majority of the discussions made hereunder were based on our summary works on the subjects of PSS (including non-progressive brain lesions like TBI), MS and CP (suggested readings given). We also incorporated the recently published practice guidelines on the use of BoNT for adult spasticity, put forth by the American Academy of Neurology, as well as an updated systematic review of CP management (additional readings given).

5. Botulinum Toxin for Treatment Goals in Spasticity

BoNT has withstood the test of time, being an efficacious and safe symptomatic therapy for chronic spasticity, hinged from meta-analyses derived from well-conducted, randomized controlled clinical trials. Thus, BoNT, in combination with neurorehabilitation, is considered a first
line treatment in focal and multifocal spasticity, both in adults and children. Pharmacologic BoNT presynaptic cholinergic blockading effects may be seen not only in extrafusal muscles, but also the intrafusal muscles, leading to a modulation of afferent signals to the spinal and supra-spinal levels. This dual blockade mechanism of action of BoNT attains clinical significance in the spasticity state where increased muscle tone and stretch reflexes occur.

Targeted use of BoNT in established spasticity should be hinged on realistic goals that will facilitate reduction of muscle tone and pain, improve passive limb functions (e.g. dressing, hygiene, cosmesis) and facilitate in tandem neurorehabilitation. Goal Attainment Scaling (GAS) may be the ideal way to assess success of BoNT injection, in that the pre-defined aims are gleaned to be person-centered, realistic and achievable. Injection protocols for BoNT should be flexible and “tailor fit” for subsequent and repeat cycle injections, considering that goals may change over time. Muscle selection with avoidance of compensatory muscles, proper dosing and dilutions, appropriate injection delivery and guidance, initial and post-injection established protocols and awareness of contraindicated disorders (e.g. neuromuscular junction disorders) should all factor in, to optimize efficacy. Improvement in active function (not so achievable to date) with established upper limb spasticity is a fair desire from both the patient and the clinician, however, one may have to incorporate the injections with an interdisciplinary team approach. In CP, patients who are malnourished and who are having oropharyngeal dysfunction, pseudobulbar palsy and a high Gross Motor Function Classification (GMFCS) level are considered a high risk group for BoNT injection complications. In the case of MS, being an immune-mediated process, reviews state a principal suitability of BoNT for treatment of spasticity. An added benefit could be explored on how BoNT may potentially impact on the accompanying pain in MS, other than spasticity. Included in this present book are dedicated chapters on instrumentation-guided BoNT injections and rehabilitation practices in adults and children with spasticity.

6. Botulinum Toxin For Spasticity and its Associated Impairments

BoNT is a powerful treatment to address associated spasticity impairments, in that the toxin could be targeted to a muscle or muscle groups. These impairments are:

1. Spastic co-contraction: inappropriate antagonist recruitment brought about by the volitional command on an agonist, while stretch is absent. Possibly present in usual motor movement, an excessive simultaneous co-activation of agonist and antagonist muscles in spastic paresis may occur. Muscle over-activity may predominate in some muscles in spastic paresis, causing agonist-antagonist imbalance. BoNT may potentially restore the balance around joints by focally reducing muscle over activity;

2. Spastic dystonia: stretch-sensitive tonic muscle contraction in the absence of voluntary command to adjacent muscles and in the absence of phasic stretch of the affected muscles. As a consequence, it may alter the resting posture, while contributing to deformity and impairment of passive function. BoNT targeted to over-active muscle groups,
together with muscle lengthening, could raise stretch receptor recruitment threshold in the affected muscles and therefore reduce the severity of these potentially disabling forms of over-activity. In fact, it may well be, that this could be the best indication for BoNT injection as it addresses both phenomena of spasticity and dystonia altogether;

(3) Associated reactions: abnormal postural reactions (usually in upper limbs) seen on the hemiplegic side. These movements may posturally affect movement, as these are purposeless. Past BoNT studies targeting these undesired movements have allowed more gain in functionality amongst affected individuals, and in fact, the said improvement may become a measure of patient progression;

(4) Local biomechanical changes and contractures: musculo-skeletal mechanical changes occurring during early immobilization in an upper motor neuron syndrome that may augment resistance to passive movements, potentially increasing resting discharge of muscle spindles and eventually their stretch sensitivity. Left unattended, muscle contracture occurs by similar adaptations. In these subset of patients, muscle contracture contributes significantly to hypertonia. BoNT early injections in PSS and non-progressive brain lesions (<3 months), potentially modify the course of spasticity evolution, and perhaps prevent the disabling consequences of immobilization and contracture.

7. Optimization of bont effects in spasticity

The American Academy of Neurology gave a Grade A recommendation for BoNT in the treatment of spasticity in adults and in spasticity in CP. Together with neurorehabilitation, BoNT injections into the shorter of the two co-contracting muscles around the joint can augment stretching activities. Evidences exist on how BoNT injections indirectly modulate sensorimotor loops at the spinal and supra-spinal levels and to which end, it has the capability to modify the course and progression of spasticity, especially in early PSS interventions. The goals do change in chronic spasticity and the person-centered GAS, has been proven to optimize BoNT effects, under time-monitored endpoints.

The optimal time to best administer BoNT in either or both affected hemiparetic limbs, would be when spasticity becomes established, impeding passive and active functions, occurrence of associated reactions and pain, while impairing patient quality of life (as is true with carer burden). On the other hand, early BoNT injections potentially extend window time for motor re-learning with physiotherapy. In effect, the early BoNT intervention paradigm may potentially modify the natural progress of spasticity, prevent spasticity/dystonia-related complications or even delay re-injection.

Interestingly, a multi-modal therapeutic approach in spasticity will likely be a good model for optimizing care. Among others, those that are promising include combining BoNT injections with the following: (a) intensive occupational therapy and low-frequency repetitive transcranial magnetic stimulation; (b) constraint-induced movement therapy; and (c) high intensity ambulatory rehabilitation programs.
8. Conclusion and recommendation

Spasticity often requires consequent treatment. Therapeutic nihilism may produce devastating long-term complications. An interdisciplinary approach combines BoNT and rehabilitation. Recommendations are robust on the use of BoNT as a symptomatic therapy for PSS, non-progressive brain lesions, CP and MS. Carefully defined treatment goals are pivotal to achieve optimal outcomes and to optimize care practices. After developing the injection scheme, correct BoNT placement into the target muscles remains a major challenge. Recommended practice points to take home, when applying BoNT in spasticity, are summarized in the Table.

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Recommended 10-Point Practice Guides in Botulinum toxin Injections (BoNT) for Spasticity:

1. BoNT injections are given strong recommendations for spasticity after stroke and non-progressive brain lesions, multiple sclerosis and cerebral palsy;
2. BoNT therapy is best indicated (based on contemporary guidelines) in chronic focal spasticity to reduce hypertonicity (and pain), improvement in disability (passive more than active functions), patient (and care-giver) quality of life and realistic person-centered goals;
3. BoNT early interventions protocols (< 3 months from ictus) may modify spasticity progression, prevent contracture and delay re-injection;
4. BoNT therapy may potentially restore the balance around joints by focally reducing muscle over-activity in spastic co-contraction, spastic dystonia and associated reactions;
5. BoNT therapy should be part of a multi-modal or tandem neurorehabilitation practices to optimize achievement of goals;
6. BoNT injections should be flexible and “tailor fit” for subsequent and repeat cycle injections, considering that goals may change;
7. BoNT targeting, while applying appropriate and timely muscle selections, are key elements in injection success;
8. BoNT delivery by instrumentation-guidance (e.g. ultrasound, electromyography and electrical stimulation) may further optimize injection practices;
9. BoNT correct dosing and appropriate dilutions are important guides during injections (e.g. “high potency, low dilutions” to localize/maximize desired effects in small forearm and hand and foot muscles; “low potency, high dilutions” intended to spread the toxin in large arm, thigh and leg muscles);
10. BoNT caveats in injection include: over-enthused injections in spasticity-protective muscles (e.g. postural thigh muscles), compensatory muscles, concomitant neuromuscular junction disorders, frail and malnourished children or those with high Gross Motor Function Classification System.
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Suggested readings


Additional references
