BoNT in Cranial Dystonia-
Blepharospasm, Hemifacial Spasm,
Oromandibular and Laryngeal Dystonia

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Disclosures

• None
Outline

• Evidence-Based Recommendations
• Overview of Management of Dystonia
• Blepharospasm
• Hemifacial Spasm
• Oromandibular Dystonia
• Laryngeal Dystonia
• Dosage Guidance
• Conclusions
### Evidence-Based Recommendations

#### Table 2: Evidence-based conclusions and recommendations for the efficacy of various botulinum neurotoxin formulations by indication

<table>
<thead>
<tr>
<th>Indication</th>
<th>Level A&lt;sup&gt;a&lt;/sup&gt; effective</th>
<th>Level B&lt;sup&gt;b&lt;/sup&gt; probably effective</th>
<th>Level C&lt;sup&gt;c&lt;/sup&gt; possibly effective</th>
<th>Level U&lt;sup&gt;d&lt;/sup&gt; insufficient evidence</th>
<th>Level A&lt;sup&gt;e&lt;/sup&gt; ineffective</th>
<th>Level B&lt;sup&gt;f&lt;/sup&gt; ineffective</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blepharospasm</td>
<td>OnabotulinumtoxinA</td>
<td>AbobotulinumtoxinA</td>
<td>RimabotulinumtoxinB</td>
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<td>Cervical dystonia</td>
<td>AbobotulinumtoxinA,</td>
<td>OnabotulinumtoxinA,</td>
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<tr>
<td></td>
<td>rimabotulinumtoxinB</td>
<td>incobotulinumtoxinA</td>
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<td>Upper limb spasticity&lt;sup&gt;g&lt;/sup&gt;</td>
<td>AbobotulinumtoxinA,</td>
<td>OnabotulinumtoxinA,</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>onabotulinumtoxinA&lt;sub&gt;h&lt;/sub&gt;,</td>
<td>incobotulinumtoxinA</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>incobotulinumtoxinA&lt;sub&gt;i&lt;/sub&gt;</td>
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<td></td>
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<td>Lower limb spasticity</td>
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<td>abobotulinumtoxinA</td>
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<tr>
<td>Chronic migraine</td>
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<td>OnabotulinumtoxinA</td>
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<tr>
<td>Episodic migraine</td>
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<td></td>
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<tr>
<td>Tension-type headache</td>
<td>OnabotulinumtoxinA</td>
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<td></td>
<td>OnabotulinumtoxinA</td>
</tr>
</tbody>
</table>

Simpson et al. Neurology 2016;86:1818
# Evidence-Based Recommendations

Table 1. Levels of Evidence for Botulinum Treatment of Focal Dystonia.

<table>
<thead>
<tr>
<th>Botulinum Toxin (Strain)</th>
<th>Focal Dystonia Subtype</th>
<th>Level of Evidence</th>
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</thead>
<tbody>
<tr>
<td>Onabotulinum (A)</td>
<td>Blepharospasm</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td>Oromandibular dystonia</td>
<td>C</td>
</tr>
<tr>
<td>Abobotulinum (A)</td>
<td>Blepharospasm</td>
<td>C</td>
</tr>
<tr>
<td></td>
<td>Oromandibular dystonia</td>
<td>C</td>
</tr>
<tr>
<td>Incobotulinum (A)</td>
<td>Blepharospasm</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td>Oromandibular dystonia</td>
<td>U</td>
</tr>
<tr>
<td>Rimabotulinum (B)</td>
<td>Blepharospasm</td>
<td>U</td>
</tr>
<tr>
<td></td>
<td>Oromandibular dystonia</td>
<td>U</td>
</tr>
</tbody>
</table>

A—Effective; B—Probably Effective; C—Possibly Effective; U—Insufficient Evidence Adapted from [25].

Hassell and Charles. Toxins 2020;12:0269
Overview of Management of Dystonia

Jinnah et al. Neurol Clin 2020;38:325
Blepharospasm

- Clinical spectrum ranges from excessive blinking to functional blindness in 15% of cases
- Very few patients improve with anticholinergics or clonazepam
- No effective surgery
- BoNT injections
  - Improve 90% of patients for an average of 3.5 months
  - Complications: ptosis, excessive tearing, diplopia, others

Defazio et al. Mov Disord 2017;32:498
Blepharospasm

- Frontalis
- Procerus
- Obicularis oculi
- Corrugator superciliii
-levator
Blepharospasm
Hemifacial Spasm

- A peripheral myoclonus, NOT a focal dystonia
- Vascular compression of the facial nerve
- Association with arterial hypertension
- Granulomas and tumors are rare causes
- Rare patients respond to antiepileptic agents
- Vascular decompression
  - 60-90% of patients improve
  - Recurrence is not infrequent
  - Surgical complications may include facial palsy, deafness, stroke

Oliveira et al. Mov Disord 1999;14:832
Hemifacial Spasm

• BoNT injections
  • Improve 90% of patients
  • Average duration of response is 3 months
  • Most common complications
    • Ptosis,
    • Excessive tearing
    • Diplopia
    • Facial asymmetry
  • As there is simultaneous weakness, contralateral injections are necessary to prevent facial asymmetry

Oliveira et al. Mov Disord 1999;14:832
Pretarsal versus Preseptal Palpebral Injections

Comparison of Techniques of Botulinum Toxin Injections for Blepharospasm and Hemifacial Spasm

Botulinum toxin (BTX) injections are the treatment of choice for blepharospasm (BSP) and hemifacial spasm (HFS). There is, however, no agreement on which is the best injection technique. Çakmur and colleagues proposed that the pretarsal technique had a longer therapeutic duration and a better side effect profile than preseptal injections. One prospective and randomized trial compared 4 different injection techniques (pretarsal, inner orbital, outer orbital, and brow) for BSP, demonstrating a longer effect duration of the pretarsal technique.

Comparing a triple technique into the orbicularis oculi, another study suggested that the outcome is improved after adding a pretarsal injection. In a double-blind, prospective study of treatment for BSP and HFS, the pretarsal technique also had a longer effect duration. Mostly because of methodological issues, these studies have not settled the question of the most appropriate injection technique for the BTX treatment of BSP and HFS.

In conclusion, our study shows that the efficacy and tolerability of pretarsal and preseptal BTX injections to treat BSP and HFS are comparable. The former technique has a longer duration of effect that may account for patient preference.

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Sacramento et al. Mov. Disord. 2019;34:1401
Oromandibular Dystonia

• Focal dystonia of the masticatory, lower facial and lingual muscles

• Patterns
  • Jaw Closing
  • Jaw Opening
  • Lateral Deviation
  • Mixed

• Etiology
  • Idiopathic
  • Tardive
  • Stroke
  • Genetic – Wilson’s disease, NBIA...
Oromandibular Dystonia

- Baclofen, tetrabenazine, zolpidem or anticholinergics rarely improve patients
- BoNT injections
  - Improvement in 50-70%
  - Jaw closing pattern has better response than jaw opening dystonia
  - EMG or ultrasound guidance may be necessary to inject pterygoid muscles
  - Dysphagia and local pain are the most common complications

Hassell and Charles. Toxins 2020;12:0269
Laryngeal Dystonia (Spasmodic Dysphonia)

• Focal dystonia of the vocal cords
• Adductor and abductor types
• Refractory to any drug or speech therapy
• BoNT injections:
  • Always EMG-guided
  • Uni or bilateral injections
  • 90% of subjects improve for an average of 5 months
  • Hoarseness and dysphagia are the most common complications
Proposed Conversion of Different Types of Botulinum Toxin A

1U OnabotulinumtoxinA = 1U IncobotulinumtoxinA
1U OnabotulinumtoxinA = 2.5U AbobotulinumtoxinA

<table>
<thead>
<tr>
<th>Site</th>
<th>Mean Dose</th>
<th>SD</th>
<th>(Range)</th>
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</thead>
<tbody>
<tr>
<td>B</td>
<td>7.9</td>
<td>3.2</td>
<td>(5-20)</td>
</tr>
<tr>
<td>L</td>
<td>11.5</td>
<td>2.5</td>
<td>(5-25)</td>
</tr>
<tr>
<td>M</td>
<td>51.9</td>
<td>23.1</td>
<td>(10-150)</td>
</tr>
<tr>
<td>SC</td>
<td>98.8</td>
<td>26.2</td>
<td>(50-150)</td>
</tr>
<tr>
<td>SCM</td>
<td>93.5</td>
<td>35.8</td>
<td>(10-200)</td>
</tr>
<tr>
<td>SM</td>
<td>29.2</td>
<td>12.5</td>
<td>(10-75)</td>
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<tr>
<td>SP</td>
<td>116.6</td>
<td>31.4</td>
<td>(25-200)</td>
</tr>
<tr>
<td>T</td>
<td>99.7</td>
<td>27.1</td>
<td>(25-200)</td>
</tr>
<tr>
<td>V</td>
<td>29.7</td>
<td>6.2</td>
<td>(15-50)</td>
</tr>
</tbody>
</table>

*Figure 1  Botulinum toxin: location of injections and dose per muscle. B = eyebrow, L = eyelid (orbicularis oculi), M = masseter, SC = zygomaticus, SCM = sternocleidomastoid, SM = submental, SP = splenius capitis, T = trapezius, V = vocalis complex.*

Jankovic et al. J Neurol Neurosurg Psychiatry 1999;53:633
Conclusions

• Cranial dystonia is etiologically and phenomenologically heterogeneous

• Pharmacological treatment of cranial dystonia is usually ineffective

• Although the level of evidence is relatively low, BoNT injections are the treatment of choice of cranial dystonia

• Most patients have a good response with few side effects
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Prof. Sarah Camargos
Dr. Débora Maia
Dr. Mauro Cunningham
Dr. Ricardo Maciel
Dr. Nina Rosa