Botulinum toxin injection following deep brain stimulation in generalized dystonia

Barbara I. Karp*, Vesper Fe Marie Llaneza Ramos, Katharine Alter and Codrin Lungu

1CNS, IRB, National Institutes of Health, Bethesda, MD-20892, USA
2Human Motor Control Section, National Institutes of Health, Bethesda, MD-20892, USA
3Functional and Applied Biomechanics Section, Rehabilitation Medicine Department, National Institutes of Health, Bethesda, MD and Mount Washington Pediatric Hospital, Washington, DC, USA
4Office of the Clinical Director, National Institutes of Health, Bethesda, MD-20892, USA

Introduction

Deep brain stimulation (DBS) has emerged as an effective treatment for idiopathic generalized and some focal dystonias [1,2]. It is also increasingly utilized in patients with symptomatic or secondary dystonias, such as those due to cerebral palsy, post-traumatic dystonia, post-stroke dystonia, tardive dystonia, neurodegenerative or metabolic disorders such as pantothenate [3], kinase-associated neurodegeneration (PKAN), and other disorders, although they may be less responsive to DBS [1,4-8].

For dystonia, DBS usually targets the GPi and is often reserved for patients who are poorly controlled with oral medications and botulinum toxin (BoNT) injections. DBS typically improves generalized dystonia by about 50% on rating scales such as the Burke-Fahn-Marsden dystonia rating scale [1,9].

BoNT plays a limited role in management of generalized dystonia as toxic doses would be required to treat all body areas. However, BoNT can successfully relieve spasm in discrete body areas [9-11]. Patients with generalized dystonia often receive BoNT injections for symptomatic control of specific symptoms before undergoing DBS. Since residual symptoms are present in patients with generalized dystonia following DBS, continuing BoNT injections after DBS placement may be helpful. There is, however, little literature available on the utility of botulinum toxin after DBS surgery and whether the dose, selection of muscles or response to BoNT is altered by DBS. In this small retrospective study, we evaluated the utility of BoNT following DBS surgery in patients with generalized dystonia.

Methods

The National Institute of Neurological Disorders and Stroke Human Motor Control Section clinical database was queried for patients with generalized dystonia who received BoNT injections for at least 1 year after DBS. The muscles injected, BoNT dose, and response to injection were recorded for the last injection session prior to DBS (when applicable) and followed yearly from date of DBS surgery (Table 1).

Results are described as mean (range). Response to BoNT was scored using a patient self-reported visual analog scale ranging from 0% (no improvement) to 100% (no dystonic symptoms). DBS settings were adjusted during the period of BoNT treatment by patient physicians independent of those injecting BoNT.
Table 1. Number of muscles and doses before and annually after DBS.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Time of injection</th>
<th>Muscles</th>
<th>Total dose*</th>
<th>Response**</th>
</tr>
</thead>
<tbody>
<tr>
<td>DYT1</td>
<td>Before DBS</td>
<td>9</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>1 y</td>
<td>5</td>
<td>500</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>2 y</td>
<td>5</td>
<td>500</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Intrauterine Rubella</td>
<td>Before DBS</td>
<td>4</td>
<td>200</td>
<td>0</td>
</tr>
<tr>
<td>0y (immediately p-dbs)</td>
<td>4</td>
<td>320</td>
<td>75</td>
<td></td>
</tr>
<tr>
<td>1 y</td>
<td>8</td>
<td>300</td>
<td>75</td>
<td></td>
</tr>
<tr>
<td>2 y</td>
<td>9</td>
<td>500</td>
<td>75</td>
<td></td>
</tr>
<tr>
<td>3 y</td>
<td>7</td>
<td>370</td>
<td>75</td>
<td></td>
</tr>
<tr>
<td>4 y</td>
<td>6</td>
<td>360</td>
<td>75</td>
<td></td>
</tr>
<tr>
<td>5 y</td>
<td>6</td>
<td>310</td>
<td>75</td>
<td></td>
</tr>
<tr>
<td>6 y</td>
<td>7</td>
<td>330</td>
<td>75</td>
<td></td>
</tr>
<tr>
<td>7 y</td>
<td>3</td>
<td>320</td>
<td>75</td>
<td></td>
</tr>
<tr>
<td>PKAN2</td>
<td>Before DBS</td>
<td>9</td>
<td>20</td>
<td>25</td>
</tr>
<tr>
<td>1 y</td>
<td>215</td>
<td>0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* dose = units onabotulinumtoxinA
** Response assessed by patient/family as % improved (0=none to 100= complete response)

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an ancestry, with otherwise normal birth and delivery and early childhood milestones, was diagnosed as having a psychogenic movement disorder when she developed abnormal hand and feet posturing at age 10. Symptoms worsened despite psychiatric therapy and neurologic therapy, including trial of benzodiazepines, antidepressants, levodopa, baclofen and trihexiphenidyl, such that by age 24, dystonia had generalized to involve the trunk and all extremities and she required a wheelchair. Genetic testing was positive for DYT1. She had GPI DBS initiated at age 30. BoNT injections were first started after DBS to address residual dystonic symptoms. Over the next 6 years, she received a mean dose 627 units (range 200-785) with a stable response rated 50 ± 8% improvement. She has reported no adverse effects of injection.

Discussion

While the first line treatment for focal dystonia, botulinum toxin injection is not uncommonly used in patients with generalized dystonia to address focally disabling symptoms. GPI DBS, however, is a better approach for these patients, reducing generalized dystonic symptoms by 50-80% and improving quality of life, comfort and function [1,9]. Although patients with generalized dystonia that is acquired or due to a degenerative underlying disease have a less robust response to DBS, they often benefit sufficiently to justify the risks of surgery [7]. DBS is increasingly being used in this population. Both BoNT injections and DBS offer the advantage of being safe to use in combination with other therapeutic modalities, including each other. The lack of published literature on the utility of botulinum toxin injection after DBS implantation leaves little to guide physicians on their combined use.

This report of 4 cases, 2 patients with DYT-1 dystonia, 1 with acquired dystonia from perinatal infection and 1 with dystonia due to the neurodegenerative disease PKAN, provides the first information on the utility of BoNT in combination with DBS. Although we have followed only a small number of patients receiving BoNT after DBS for generalized dystonia, their cases are informative. These patients show that botulinum toxin can continue to be effective in managing residual dystonic symptoms over up to at least 7 years and that the dose and response can remain stable with DBS, including stimulator setting adjustments. Further study is needed to better delineate the role for BoNT in management of dystonia in combination with DBS.

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References


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