Botulinum Toxin in The Treatment of Dystonias — A Hospital Based Study

Meena Gupta,* G Singh,** Geeta Khwaja*

Abstract
Background : Dystonia is a neurological disorder usually of idiopathic etiology with a wide spectrum of clinical manifestations. The advent of botulinum toxin has revolutionized the treatment of focal dystonias. This study was a prospective long term study to see the efficacy of botulinum toxin in the treatment of dystonias.

Material and Methods : There were a total of 215 injection sessions of botulinum toxin during a period of 4 years and 8 months. Patients were evaluated in detail and their severity of dystonias was graded on objective scales. Botulinum toxin injection were administered depending on the type and severity of dystonias. The response to treatment was gauged in terms of latency, and the degree and duration of improvement. The dosages were repeated as and when required, with minimal interval of 3 months.

Results : We had a total number of 215 injection sessions, with maximum patient sessions with blepharospasm and hemifacial spasm (59 and 61, respectively). The lowest dosages of botulinum toxin were required for writer’s cramps and blepharospasm (92.5 ± 5.3; and 122 ± 5.1) while highest dosages were required for generalized and cervical dystonias (512 ± 10.5; and 452.5 ± 8.5). The best response in terms of different parameters assessed was seen with blepharospasm and hemifacial spasm while it was lowest for the generalized dystonia group. We did not observe any declining responsiveness to botulinum toxin with repeated injections. The side effects were minimal and self-limiting.

Conclusion : Botulinum toxin injection is an effective and safe modality for the treatment of disabling dystonias. Cost is one of the major hinderances to its widespread use.

INTRODUCTION

Dystonia is a neurological disorder characterized by involuntary, repetitive or sustained muscle contractions frequently causing twisting, squeezing or other movements, and abnormal postures.1 In most patients, no specific cause for the dystonia can be identified. Also, the neurochemicals mechanisms of dystonias are not well understood and hence pharmacologic therapy is unsatisfactory in majority of patients. The advent of botulinum toxin has revolutionized the treatment of dystonias. A potent neurotoxin, botulinum toxin acts at peripheral cholinergic synapses and blocks the release of acetylcholine. Botulinum toxin is now one of the foremost treatment modalities of various types of focal dystonias. Although expensive, it is one of the safest treatment options for various disabling dystonias. We present the results of long-term prospective study of botulinum toxin in various types of focal and generalized dystonias at our center and attempt to define its role in the long-term management of these patients.

MATERIAL AND METHODS

The patients with focal, segmental and multisegmental dystonia were identified in this study. To be included in the study, patient must have had a disabling dystonia despite being on therapy. All the patients were examined in detail and presence of other associated causes of dystonias were looked for. The dystonias were graded at the time of injection; and severity and functional status was determined (if applicable) at the time of injection. After each injection, patients were asked to come for follow up regularly and efficacy as well as side effects were noted.

The severity of dystonias was rated on 0 to 4 scale.1

0 - no spasm; no dystonia
1 - mildly, barely noticeable
2 - mild, without functional impairment

*Professor; **Senior Resident, Department of Neurology, G.B. Pant Hospital, New Delhi - 110 002.
Received : 26.6.2002; Accepted : 25.12.2002
3 - moderate spasm, with moderate functional impairment
4 - severe, incapacitating spasm

For writer’s cramps, the functional status was assessed on the basis of a scoring system decided by observing the writing sample.2

0 - totally illegible
1 - some words illegible
2 - all words legible but some with difficulty
3 - all words legible

For blepharospasm and hemifacial spasm, functional status was decided at the day of injection as shown below: 3

<table>
<thead>
<tr>
<th>Functional Status</th>
<th>Visual Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Blind</td>
<td>Dependent outside</td>
</tr>
<tr>
<td>2 Independent, poor function</td>
<td>Independent, moderate function</td>
</tr>
<tr>
<td>3 Inconvenienced</td>
<td>Normal</td>
</tr>
</tbody>
</table>

The patients were asked to come for follow up on a regular basis and were advised repeat injections of botox (repeat only after 3 months) if the patient’s symptoms or functional impairment (as perceived by patients) warranted. However, injections were not repeated at less than three months interval. As the patients were followed, the following parameters were noticed.1

**Latency**

Interval (in days) between the injection and the first sign of improvement following the injection.

**Peak Effect**

The maximum benefit obtained from the injection, rated on 0 - 4 scale.

0 - no effect
1 - mild improvement
2 - moderate improvement, but no change in function
3 - moderate improvement in severity and function
4 - marked improvement in severity and function

* Global rating was a measure of overall response and was measured as
  * Peak effect minus One: if there were mild side effects
  * Peak effect minus Two: if there were disabling side effects

Patient with global ratings of ≥ 2 were considered to have a favorable response.

**Maximum Duration of Improvement**

Number of weeks during which patient had peak effect.

**Total Duration of Improvement**

Entire period (in weeks) during which patient noted any improvement and following which botulinum toxin injections were required.

In patients who had more than one kind of dystonias, the severity of each was graded separately and similarly, assessment of each was done independently.

**Botulinum Toxin Injection**

Botulinum toxin type A (Dysport) was used. The vials were stored frozen and toxin was reconstituted with 0.9% normal saline. The potency of toxin is determined in terms of mouse units, where one unit (u) of toxin equals approximately 0.4 ng of protein toxin.

**Injection Techniques**

The injections were put after cleaning the areas with normal saline and putting the injection into the muscle directly by palpating the muscle. A clinical judgment was used to decide the site of injection. The various muscles used for injections, according to the dystonias, were as follows.

- **Blepharospasm**: Orbicularis oculi
- **Hemifacial spasm**: Local injection into muscle, which contracted most (orbicularis oculi, mentalis, platysma). Orbicularis oris was, however, not injected.
- **Oromandibular dystonias**: Masseter, temporalis, submental and suprasyloid
- **Torticollis**: Sternocleidomastoid + contralateral trapezius
- **Laterocollis**: Ipsilateral splenius capitis, trapezius and scalenus medius
- **Anterocollis**: Both sternocleidomastoids
- **Writer’s cramp**: The patients were injected into most actively contracting muscles.
- **Generalized dystonias**: They were injected into the most affected parts.

The dosage of botulinum toxin was decided on the basis of types of dystonia, muscle mass and also, the severity of dystonia [as described in earlier studies by Jancovic, Jancovic and Brin et al]. In the case of larger neck muscles, the total dose was distributed in four to six injections. It is to be understood that there were two commercial forms of botulinum toxin available - one is Botox and second is Dysport. Clinically, observable activity of 1 unit of Botox is roughly equivalent to 3-4 units of Dysport.5

**RESULTS**

We had a total of 215 sessions of botulinum toxin injections during a period of 4 years and 8 months. The age and sex distribution along with the duration of symptoms and prior treatment is as shown in Table 1. Table 2 - 4 depict the severity distribution of the dystonias among different subgroups while Table 5 shows the overall outcome and responsiveness. As evident, the maximum number of injection sessions were received by patients with hemifacial spasm and blepharospasm while we had one session each with unilateral limb tremor, head tremor and hemidystonia. Majority of our patients were already on medical therapy. The medical therapy comprised of either of the following...
drugs: anticholinergics (trihexyphenidyl), benzodiazepines, clonazepam, baclofen, alprazolam or carbamazepine. Out of these, anticholinergics were the most frequently prescribed drugs. Most of these drugs were partially effective in the initial few months of the illness.

**Blepharospasm**

There were 59 botulinum toxin injection sessions. Mean age of the patients was 45.2 years, with male to female ratio of 7:5. The mean duration of symptoms was 4.3 years. The majority of the patients were impaired functionally to a significant extent (31 out of 59 were in grade 4 and 23 were in grade 3). None of the patient, at the time of injection, was in functional status 5 or 6.

The mean dosage used was 122 units for each affected eye. The patients were followed up for an average of 4.3 years. The response in majority of patients was good. The mean period of latency was 3.12 days with 57 out of 59

### Table 1

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Mean age (yrs)</th>
<th>Sex ratio (M:F)</th>
<th>Mean duration of symptoms (yrs.)</th>
<th>No. of treatment session</th>
<th>Percentage of patients receiving other drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Blepharospasm</td>
<td>45.2 ± 6.79</td>
<td>7:5</td>
<td>4.3 ± 0.9</td>
<td>59</td>
<td>Trihexyphenidyl: 83.3% Clonazepam: 75% Carbamazepine: 16.6% Alprazolam: 8.3%</td>
</tr>
<tr>
<td>2. Hemifacial spasm</td>
<td>46.5 ± 7.12</td>
<td>7:8</td>
<td>6.2 ± 1.2</td>
<td>62</td>
<td>Trihexyphenidyl: 86.6% Clonazepam: 73.3% Carbamazepine: 13.3% Alprazolam: 26.6%</td>
</tr>
<tr>
<td>3. Writer’s cramps</td>
<td>39.7 ± 8.12</td>
<td>6:1</td>
<td>4.9 ± 0.9</td>
<td>35</td>
<td>Trihexyphenidyl: 92% Clonazepam: 78% Baclofen: 21.4% Alprazolam: 14.2%</td>
</tr>
<tr>
<td>4. Cervical dystonia</td>
<td>44.2 ± 9.12</td>
<td>12:1</td>
<td>5.4 ± 1.1</td>
<td>24</td>
<td>Trihexyphenidyl: 84.6% Clonazepam: 76.9% Baclofen: 23.7% Carbamazepine: 7.69% Alprazolam: 15.38% Syndopa: 7.69%</td>
</tr>
<tr>
<td>5. Oromandibular dystonia</td>
<td>47.2 ± 8.64</td>
<td>4:1</td>
<td>2.4 ± 0.6</td>
<td>9</td>
<td>Pacitane: 60% Clonazepam: 61% Carbamazepine: 20% Syndopa: 85% Pacitane: 66.6% Clonazepam: 66.6% Baclofen: 33.3% Propranolol: 33.3%</td>
</tr>
<tr>
<td>6. Generalized dystonia</td>
<td>28.8 ± 8.92</td>
<td>2:1</td>
<td>7.8 ± 1.1</td>
<td>18</td>
<td>Syndopa: 85% Pacitane: 66.6% Clonazepam: 66.6% Baclofen: 33.3% Propranolol: 33.3%</td>
</tr>
</tbody>
</table>

**Miscellaneous**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Mean age (yrs)</th>
<th>Sex ratio (M:F)</th>
<th>Mean duration of symptoms (yrs.)</th>
<th>No. of treatment session</th>
<th>Percentage of patients receiving other drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>7. Essential termor</td>
<td>49</td>
<td>1:0</td>
<td>25</td>
<td>6</td>
<td>Trihexyphenidyl</td>
</tr>
<tr>
<td>8. U/L limb tremor</td>
<td>54</td>
<td>1:0</td>
<td>1</td>
<td>1</td>
<td>Clonazepam</td>
</tr>
<tr>
<td>9. Hemidystonia</td>
<td>58</td>
<td>1:0</td>
<td>4</td>
<td>1</td>
<td>Clonazepam</td>
</tr>
</tbody>
</table>

### Table 2: Severity of dystonias

<table>
<thead>
<tr>
<th>Severity</th>
<th>Cervical dystonia</th>
<th>Oromandibular dystonia</th>
<th>Generalized dystonia</th>
<th>Essential tremor</th>
<th>U/L limb tremor</th>
<th>Left hemidystonia</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>1</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>3</td>
<td>20</td>
<td>7</td>
<td>15</td>
<td>—</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>2</td>
<td>—</td>
<td>2</td>
<td>1</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

### Table 3: Functional status distribution for hemifacial and blepharospasm (Decreasing severity)

<table>
<thead>
<tr>
<th>Functional status</th>
<th>Hemifacial spasm</th>
<th>Blepharospasm</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>32</td>
<td>23</td>
</tr>
<tr>
<td>4</td>
<td>25</td>
<td>31</td>
</tr>
<tr>
<td>5</td>
<td>1</td>
<td>—</td>
</tr>
<tr>
<td>6</td>
<td>0</td>
<td>—</td>
</tr>
</tbody>
</table>

### Table 4: Functional status distribution for writer's cramps

<table>
<thead>
<tr>
<th>Functional status</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>1</td>
<td>26</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
</tr>
</tbody>
</table>
sessions resulting in moderate to marked improvement in severity and function. The average peak effect (3.51) was maximum in this group, with duration of maximum improvement being 9.1 weeks and mean total duration of improvement being 26.2 weeks. There were only three sessions when there were side effects. All of these were mild in the form of pain or slight ptosis, which was self-limiting. The overall favorable response² (i.e. the percentage of patients sessions having global score ≥ 2) was 98.3%. This group had overall the best response to botulinum toxin therapy.

**Hemifacial Spasm**

This was the group who received maximum botulinum toxin injections (n = 62). Mean age of the patients was 46.5 years with M:F ratio 7:8. The mean duration of symptoms was 6.2 years. Significant functional and cosmetic impairment was present in majority of patients (Table 3). The mean dosage used was 142.5 IU for one side and the patients were followed for a mean duration of 3.7 years. The minimum time to the beginning of response varied from 2-12 days with mean latency of 4.1 days. Majority of patients showed marked to moderate improvement, both in severity as well as function (59 out of 62).

This mean duration of maximum improvement was 7.9 weeks while mean total duration of improvement was 24.3 weeks. One of these patients went into remission for a duration of approximately 20 months on one occasion and then again for a duration of 14 months. Only four out of 62 sessions had some reported side effects, out of which three had pain and one had mild facial weakness. These were all self-limiting. The mean global rating was 3.39 and the percentage of patient sessions showing favourable response was 96.7%. This group combined with blepharospasm had the best response.

**Writer’s Cramp**

We had a total of 35 injection sessions with writer’s cramp patients. The mean age of the patient was 39.7 years with male:female ratio of 6:1. The mean duration of symptoms was 4.9 years. As evident from Table 4, functional impairment was present in a major fraction of patients (34 out of 35).

The mean dosage of botulinum toxin used was 92.5 IU (lowest mean dosage out of all dystonias). The patients were

---

**Table 5**

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Diagnosis</th>
<th>No. of injection session</th>
<th>Mean dosage (IU)</th>
<th>Mean duration of follow up (yrs.)</th>
<th>Mean latency (days)</th>
<th>Mean peak effect</th>
<th>No. of patient’s sessions</th>
<th>Peak effect score</th>
<th>No. of sessions with side effects</th>
<th>Severity of side effects</th>
<th>Mean max. duration of improvement (wks)</th>
<th>Mean total duration of improvement (wks)</th>
<th>Global rating score sessions</th>
<th>Global rating mean</th>
<th>Favorable response</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Blepharospasm</td>
<td>59</td>
<td>122 ± 5.1</td>
<td>4.3 ± 1.1</td>
<td>3.12 ± 1.1</td>
<td>3.51</td>
<td>32</td>
<td>4</td>
<td>—</td>
<td>—</td>
<td>9.1 ± 3.51</td>
<td>26.2 ± 4.6</td>
<td>4:32</td>
<td>2:3</td>
<td>98.3%</td>
</tr>
<tr>
<td>2</td>
<td>Hemifacial spasm</td>
<td>62</td>
<td>142.5 ± 6.2</td>
<td>3.7 ± 0.8</td>
<td>4.1 ± 1.4</td>
<td>3.47</td>
<td>32</td>
<td>4</td>
<td>1</td>
<td>Mild</td>
<td>7.9 ± 1.22</td>
<td>24.3 ± 4.1</td>
<td>4:31</td>
<td>2:3</td>
<td>96.7%</td>
</tr>
<tr>
<td>3</td>
<td>Writer’s cramp</td>
<td>35</td>
<td>92.5 ± 5.3</td>
<td>3.9 ± 0.9</td>
<td>5.6 ± 1.5</td>
<td>3.37</td>
<td>15</td>
<td>4</td>
<td>2</td>
<td>Mild</td>
<td>7.3 ± 1.12</td>
<td>22.3 ± 3.9</td>
<td>4:13</td>
<td>3:17</td>
<td>91.4%</td>
</tr>
<tr>
<td>4</td>
<td>Oromandibular dystonia</td>
<td>9</td>
<td>182 ± 4.1</td>
<td>2.1 ± 0.5</td>
<td>7.8 ± 1.9</td>
<td>3.11</td>
<td>3</td>
<td>3</td>
<td>—</td>
<td>—</td>
<td>6.3 ± 1.22</td>
<td>15.2 ± 4.3</td>
<td>4:3</td>
<td>3:2</td>
<td>77.7%</td>
</tr>
<tr>
<td>5</td>
<td>Cervical dystonia</td>
<td>24</td>
<td>452.5 ± 8.5</td>
<td>2.9 ± 0.5</td>
<td>6.7 ± 1.6</td>
<td>3.0</td>
<td>22</td>
<td>4</td>
<td>—</td>
<td>—</td>
<td>7.2 ± 1.26</td>
<td>20.4 ± 4.1</td>
<td>4:1</td>
<td>3:20</td>
<td>91.6%</td>
</tr>
<tr>
<td>6</td>
<td>Generalized dystonia</td>
<td>18</td>
<td>512.5 ± 10.5</td>
<td>2.5 ± 0.4</td>
<td>10.3 ± 2.1</td>
<td>2.94</td>
<td>5</td>
<td>4</td>
<td>1</td>
<td>Mild</td>
<td>6.1 ± 1.26</td>
<td>13.6 ± 4.4</td>
<td>4:4</td>
<td>3:7</td>
<td>77.7%</td>
</tr>
<tr>
<td>7</td>
<td>Essential tremor</td>
<td>6</td>
<td>912.5 ± 10.5</td>
<td>3.7 ± 3.7</td>
<td>9.3 ± 1.9</td>
<td>3.17</td>
<td>2</td>
<td>3</td>
<td>—</td>
<td>—</td>
<td>6.8 ± 0.9</td>
<td>14.6 ± 3.2</td>
<td>4:2</td>
<td>3:2</td>
<td>66.6%</td>
</tr>
<tr>
<td>8</td>
<td>U/L tremor</td>
<td>1</td>
<td>400 ± 0.5</td>
<td>0.5</td>
<td>12 ± 2</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>I</td>
<td>Mild</td>
<td>6 ± 1</td>
<td>12 ± 2</td>
<td>1:1</td>
<td>1:2</td>
<td>100%</td>
</tr>
<tr>
<td>9</td>
<td>Hemidystonia</td>
<td>1</td>
<td>450 ± 0.5</td>
<td>0.5</td>
<td>11 ± 2</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>I</td>
<td>Mild</td>
<td>5 ± 1</td>
<td>10 ± 2</td>
<td>1:1</td>
<td>1:1</td>
<td>100%</td>
</tr>
</tbody>
</table>
followed for a mean duration of 3.9 years. The mean latency for improvement was 5.6 days. Out of 35 patient sessions, in 33 sessions, there was marked improvement. The mean duration of maximum improvement was 7.3 weeks while the total duration of improvement was 22.3 weeks. Out of these, one patient had a remission for a duration of 10 months while another one had it for a duration of 21/2 years. Out of 35 sessions, seven sessions were followed by side effects; out of which one was in the form of mild weakness of the forearm which resolved in 3-4 days. Rest six had pain as a side effect.

The mean global rating was 3.14; and overall 91.4% had a favourable response.

**Cervical Dystonia**

We had 24 sessions of injections with patients of cervical dystonias. The mean age of the patient was 44.2 years. The male and female ratio was 12:1. The mean duration of symptoms was 5.4 years. Majority of patients were in moderate to marked severity (22 out of 24 patient sessions were in ≥3 grade of severity). The mean dosage of botulinum toxin used was 452.5 IU. Out of cervical dystonia, torticollis and anterocollis were most common. The mean duration of follow up was 2.9 years. The latency to respond varied from as early as 4 days to 13 days, the mean latency being 6.7 days.

Almost all the patients (23 out of 24) sessions had moderate to marked improvement; although the mean duration of maximum improvement and total improvement was less than that of blepharospasm, hemifacial spasm and writer’s cramp (Mean maximum duration of improvement = 7.2 weeks; mean total duration of improvement = 20.4 weeks). Out of 24 sessions, three sessions were followed by side effects. Two were mild in the form of pain and slight weakness of neck muscles while one session was followed by difficulty in swallowing. However, this was self-limiting and improved in 3-4 days on its own. The overall mean global score was 2.83 and the percentage of favourable response was 91.6.

**Generalized Dystonia**

There were total 18 injection sessions with this group. The mean age of this group was 28.8 years (lowest of all other groups). The male female ratio was 2:1. The mean duration of symptoms was 7.8 years (highest of all other groups). Majority (85%) of this group had been on syndopa, along with other drugs. This group was most incapacitated and majority had painful dystonias. The severity of dystonia in majority (17 out of 18) was ≥3. One of these patients had post-traumatic intracranial damage while another had idiopathic dystonia. As a group, the mean dosage required was highest in this subgroup (512.5 ± 10.5). Although, from Table 5, it might seem that the dosage was maximum for patient with essential tremor, but there was only one patient in this subgroup. Hence, generalization cannot be made. Botulinum toxin was given in the most incapacitating and painful dystonic portions of the body. The mean duration of follow up was 2.5 years. The latency to respond was also maximum in this group (mean 10.3 days) while the mean peak effect was lowest (only 13 out of 18 has peak effect ≥3; mean 2.94).

The mean duration of maximum improvement was 6.1 weeks while mean total duration was 13.6 weeks. Overall, mean global score was also lowest in this group. Weakness was noted in one patient while pain was noted in four patients.

**Oromandibular Dystonia**

There were total of nine injection sessions in this particular group. The mean age of the patients was 47.2 years, with M:F ratio of 4:1. The mean duration of symptoms was 2.4 years (lowest of all other groups). In seven out of nine injection sessions, the patients had moderate impairment. The mean dosage used was 182 units and mean duration of follow up was 2.1 years. The mean latency for improvement was 7.8 days. Seven out of nine sessions were followed by moderate to marked improvement, with mean peak effect being 3.11. The mean duration for maximum improvement was 6.3 weeks while that mean for total duration of improvement was 15.2 weeks. Two out of nine sessions were followed by side effects - one had mild pain at site of injection while other had difficulty in chewing. Overall 77.7% of patients had favourable response (global rating ≥2). The mean global score was 2.77.

**Essential Tremor**

We had only one patient of essential tremor of 49 years of age, who had come with 25 years history of tremors of significant severity affecting all his daily activities. The patient received total of 6 sessions of botulinum toxin. The mean dosage of botulinum toxin used was 912.5 units and the patient was followed for a total duration of 3.7 years. The mean latency for improvement was 9.3 days. The patient had moderate to marked improvement in five out of six occasions (mean peak effect 3.17). The mean duration of maximum improvement was 6.8 weeks while mean duration of total improvement was 14.6 weeks. This patient had a remission once for a duration of 10 months. Out of these six sessions, there were side effects on two occasions. One was mild in the form of self-limiting pain, while on second occasion, it was difficult in the form of weakness of the limbs. Overall the percentage favorable response was 66.66.

We had one patient each of unilateral limb tremor and hemidystonias, who received one session of botulinum toxin each. These two patients did not come for adequate duration of follow up and hence the data is inadequate for these two patients.

The maximum patient sessions were with blepharospasm and hemifacial spasm. In terms of the distribution, majority of dystonia in our center was in males except for hemifacial spasm. The mean duration of symptoms was lowest for oromandibular dystonia, probably because of interference with eating and swallowing.

The lowest dosages were required for writer’s cramp and blepharospasm while highest dosages were required for
generalized and cervical dystonias. This is obvious, keeping in view of the size of muscles and the number of muscles required, to be injected. The mean latency was lowest for blepharospasm, closely followed by hemifacial spasm while the highest delay in improvement was noted with generalized dystonias. It could be related to the fact that in generalized dystonia, disease is much more widespread and of much greater severity. In terms of response also, the variables were most favourable towards blepharospasm and hemifacial spasm as compared to generalized dystonias in terms of global rating scores and the duration of improvement. Another important observation was that peak effect score might not exactly correlate with efficacy in terms of duration of improvement, e.g., in oromandibular dystonias, the peak effect score was higher than that of cervical dystonia group but duration of improvement was much lower than the latter (peak effect score: 3.11 vs 3.0, mean duration of improvement 15.2 wks vs 20.4 wks).

The percentage of patients who had some favorable responses (global rating score ≥ 2) was highest in blepharospasm (98.3%) while it was lowest for generalized and oromandibular dystonia subgroup (77.7%). We had only one patient of essential tremor whose favorable response was 66.6%.

The most common side effects observed were mild to moderate pain at the site of injections, followed by the weakness of the muscles injected e.g., in case of hemifacial spasm, muscle weakness presented in the form of minimal facial deviation (in one case). However, all the side effects were self-limiting and lasted for 1-2 days. The patients required only analgesics and/or reassurance.

**Discussion**

Botulinum toxin therapy has virtually revolutionized the treatment of dystonias and is one prime example of how a potent toxic molecule can be harnessed for the service of suffering human. Of the seven antigenic subtypes, only type A has been used clinically. This toxin acts by irreversibly inhibiting presynaptic release of acetylcholine. The potency of the toxin is measured in terms of mouse units, one unit of which represent LD-50 (lethal dose) of a group of 18-20 gram female Swiss-Webster mice. The dosage of the toxin required for a particular dystonia varies as per the type and severity.

Dystonias as we know, can be generalized or focal. Focal dystonias are much more commonly encountered in clinical practice. The exact etiology and the factors affecting dystonias are yet not clear but they affect the life of the patient significantly. Drugs are usually not fully effective and botulinum toxin is generally required in majority of cases.

The dosages required to effectively treat each muscle varies from study to study and among treating physician. However, there is a general agreement that high dosages (more than 400 units of Botox in a 3 months period) and frequent injections (intervals less than 3 months) of botulinum toxin should be avoided. It has also been proposed that EMG guidance of botulinum toxin injections may facilitate dose reduction, but EMG techniques are cumbersome and difficult to use; and also the results are variable and difficult to quantify. Also, there is still lack of consensus as to the necessity of EMG in all such cases.

All the patients who visited our clinic had been on medical therapy for variable duration but were not fully controlled. In fact, majority of them were significantly impaired due to their illnesses. The mean duration of symptoms was minimum for oromandibular dystonias followed by blepharospasm, while it was maximum for generalized dystonias. The probable reason could be that oromandibular dystonias interfere with eating and chewing; and blepharospasm in addition to being cosmetic nuisance, also interferes with vision. Within the blepharospasm group, the duration of symptoms was lower for females as compared to the males. The reason for this is obvious keeping in view the immediate cosmetic effects and the social embarrassment associated with it. The probable reason for the delay in generalized dystonia is that patients are generally given trials of anticholinergics and L-dopa to which they respond partially. Also, the prohibitive costs (due to large amount of botulinum toxins required for generalized dystonias) might be operative.

Another important point to highlight is that patients present for botulinum toxin when they have significant degree of dystonia (as judged by severity of dystonias or the functional status). This could be due to many factors. First and foremost is ignorance on the part of patients as well as general physicians of the availability of botulinum toxin as a modality of treatment. Second important reason is obviously the large costs involved in the treatment.

Electromyography (EMG) has been considered to be of particular use in patients with writer’s cramps. In our study, however, clinical judgment was used to decide the site of muscle injection, rather than EMG guidance. But we found that even with clinical judgment, the overall favourable response was around 91.4% in writer’s cramps. Similar, successful results have been shown by Jancovic.1

Also, while putting the injections, the dosage for larger muscle (like sternocleidomastoid) was divided into 5-6 sites. Although it has been demonstrated that injecting muscle near the middle at one or two sites achieved the same effect as injecting multiple sites, we chose to inject multiple sites because it permitted smaller volume per injection site, minimizing patient’s discomfort. After the injection, the efficacy was variable. In our study, the shortest latency was observed with blepharo- and hemifacial spasm while the largest latent period was with generalized dystonias. The reasons could be the small muscles of eyes and face and also less severe degree of disease. We also feel that higher dosages might be indicated for cervical and generalized dystonias. Similar results have been reported earlier (Jancovic; Bhaumik S). Another reason for shorter latency could be the fact that when the disease affects the vision or cosmetic looks, even slight improvements are reported earlier.
In our study, we also observed that the response rate in various terms (including peak effect, maximum duration of improvement, total duration of improvement and global rating) was highest for blepharospasm, followed by hemifacial spasm while it was lowest for generalized dystonia group. Jancovic had also found comparable results. It has also been observed in other studies that blepharospasm and hemifacial spasm given excellent results to botulinum toxin therapy. We also observed that peak effect score might represent an index for assessing the overall degree of maximum response but can not determine the total duration of response. In our study, oromandibular dystonia had higher peak effect score than cervical dystonia subgroup but mean total duration of improvement was much lower than that of latter. Although our duration of follow up was only around 5 years, we did not observe a definite declining trend in the duration of improvement. Declining responsiveness had been shown to occur in studies by Jancovic and others. We observed that peak effect score might represent an index for assessing the overall degree of maximum response but cannot determine the total duration of response. In our study, oromandibular dystonia had higher peak effect score than cervical dystonia subgroup but mean total duration of improvement was much lower than that of latter. Although our duration of follow up was only around 5 years, we did not observe a definite declining trend in the duration of improvement. Declining responsiveness had been shown to occur in studies by Jancovic, and others. We observed that peak effect score might represent an index for assessing the overall degree of maximum response but cannot determine the total duration of response.

As far as side effect profile was concerned, we did not observe any significant side effects, leading on to discontinuation of the therapy. Majority of side effects were short lasting and required only symptomatic treatment (e.g. in the form of analgesics). Side effects are supposed to be more likely when larger dosages are used and when dosages are not divided. It is important to explain to the patient before injection sessions of the possible side effects. This allows better compliance with the treatment protocol and also, less embarrassment to the patient.

To conclude, we found that botulinum toxin is useful in the treatment of various dystonias. Focal dystonias are much more responsive than generalized dystonias. Within focal dystonias, blepharospasm and hemifacial spasm are most responsive. At present, lack of awareness and prohibitive costs are main deterrent to the mode widespread use of this modality of treatment.

REFERENCES