Botulinum Toxin Type A in the Management of Oromandibular Dystonia and Bruxism

Ron Tintner and Joseph Jankovic

Oromandibular dystonia (OMD) refers to involuntary spasms of masticatory, lingual, and pharyngeal muscles. Phenomenologically, there are seven types of OMD: jaw-closing dystonia (JCD); jaw-opening dystonia (JOD); jaw-deviation dystonia (JDD); lip and perioral dystonia; lingual dystonia; pharyngeal dystonia; and combination OMD (1). OMD may be seen in isolation (focal dystonia), as part of a more widespread segmental cranial dystonia, or as part of a multisegmental or generalized dystonia. In 1910, the French neurologist Henry Meige described a syndrome, sometimes still referred to as Meige’s syndrome, that occurred predominantly in middle-aged women and consisted of spasms of the eyelids as well as contractions of the pharyngeal, jaw, and tongue muscles (2). Because Meige was not the first to describe the disorder (Horatio Wood, a Philadelphia neurologist, described facial and oromandibular dystonia in 1887) (3), the syndrome is now more accurately referred to as cranial dystonia.

The etiologies of OMD are diverse (Table 33.1). The leading cause is primary (idiopathic) dystonia, which is often associated with other dystonias, particularly cervical and cranial. Some cases of OMD may be manifestations of inherited disorders; however, DYT1 dystonia, caused by a mutation of the torsinA gene on chromosome 9q34, the most common form of inherited dystonia, rarely involves the cranial structures (4). A patient with adult-onset OMD and no obvious family history of dystonia has been reported with a mutation of the gene for GTP cyclohydrolase 1, which causes the syndrome of dopa-responsive dystonia (5). The patient responded well to treatment with L-dopa. In addition to the primary dystonias, other common causes of OMD are drugs (tardive OMD) and peripheral injury, such as dental procedures and jaw trauma (6,7).

Until the advent of botulinum toxin (BTX) therapy, systemic pharmacologic agents were the traditional mainstay of treatment for OMD. Anticholinergics (e.g., trihexyphenidyl, benztrapine), benzodiazepines (e.g., clonazepam, lorazepam, diazepam), baclofen, and tetrabenazine (which deplete dopamine and block dopamine receptors), were useful in some patients (8). Chronic systemic pharmacotherapy, however, is largely unsatisfactory because of modest improvements and frequent side effects, resulting in a low therapeutic ratio. Dental appliances have occasionally been helpful (9). There are no effective regional denervating surgical procedures, such as those used for cervical dystonia or blepharospasm. Central stereotactic surgery, such as pallidotomy (10) and deep brain stimulation (11) have been used successfully for treatment of generalized and hemidystonias, but there is no information regarding their use for more limited craniofacial dystonias. The remainder of this review focuses on regional procedures, particularly chemodenervation with BTX.

The pharmacology of BTX and the mechanisms by which this potent biologic toxin produces local chemodenervation, benefiting patients with involuntary muscular spasms such as...
TABLE 33.1. Etiology of abnormal jaw and mouth movements

**Dystonias**
- Primary (idiopathic) dystonia
- Inherited dystonia syndromes
  - X-linked dystonia parkinsonism (Lubag); locus: DYT3
  - Dopa-responsive dystonia; locus: DYT5
  - Adult-onset idiopathic torsion dystonia of mixed type; locus: DYT6
  - Focal, adult-onset idiopathic torsion dystonia; locus: DYT7
  - Adult- and juvenile-onset idiopathic torsion dystonia of mixed type and mild severity; locus: DYT13

**Secondary dystonias**
- Drug-induced (dopamine receptor-blocking drugs, levodopa, and some serotonin reuptake inhibitors)
- Anoxic brain damage
- Peripheral dystonia (posttraumatic after oro-mandibular or dental injury or surgery)
- Neurodegenerative disorders with dystonia
  - Parkinson’s disease (jaw tremor and levodopa-induced dyskinesias)
  - Multiple system atrophy (especially that caused by levodopa-induced dyskinesias)
  - Progressive supranuclear palsy
  - Huntington’s disease
- Bruxism (idiopathic, diurnal, mental retardation, neurodegenerative disorders)
- Hemimasticatory spasm
- Hemifacial spasm
- Satoyoshi’s syndrome

Those seen in OMD, are discussed elsewhere in this volume and in other reviews (12–14). Although denervation of motor endplates has been proposed as the leading mechanism of action of BTX in dystonia, including OMD (15), there are certain paradoxes about its action that are not fully explained (16). First, the clinical effect of BTX appears to continue beyond the point of inducing weakness. Second, although BTX has been thought to affect muscle spindles, it is effective in the treatment of facial spasms, even though facial muscles are void of muscle spindles (17). Third, BTX treatment decreases sensory symptoms, including premonitory sensations experienced by patients with tics and dystonia (see Chapter 32 regarding the treatment of tics with BTX). Finally, there is controversy as to the role of central effects of BTX in patients with dystonia. Transcranial magnetic stimulation of the motor cortex in patients with limb dystonia has been used to demonstrate that BTX can transiently alter intracortical inhibition (18) and normalize distorted primary motor cortex projections to hand and forearm muscles. Secondary alteration of central sensorimotor physiology and an additional primary effect on muscle spindle function are probably critical in the long-term efficacy of BTX in dystonia (19,20). To test this hypothesis directly, blockade of muscular afferents has been performed. Yoshida et al. (21) treated 13 patients with OMD resistant to pharmacotherapy or dental treatment by injecting diluted lidocaine and alcohol intramuscularly to reduce muscle spindle afferent activity. All patients reportedly showed clinical improvement after this therapy with reduced electromyographic (EMG) activities in the affected muscles. The overall subjective improvement was 57.7% ± 25.1% (mean ± SD) on a self-rating scale. There was a 70% mean improvement in JCD, which was significantly higher than the 38% improvement in JOD. This mode of therapy may turn out to be useful when more experience is obtained and should ultimately be compared directly with BTX.

**MUSCLE SELECTION**

Ideally, one should be able to determine which muscles are primarily involved in the abnormal movements, and inject these muscles with the appropriate dose of BTX, thus affecting only those actions involved in the production of the abnormal movement or posture. Table 33.2 lists

| TABLE 33.2. Muscles affecting jaw and tongue movement |
|-----------------------------------|-----------------|
| **Muscle**            | **Actions**                                      |
| Masseter              | Jaw closing                                           |
| Temporalis            | Jaw closing; anterior fibers assist in jaw opening and deviation |
| Internal pterygoid     | Jaw closing                                           |
| Digastric             | Jaw opening                                           |
| External pterygoid     | Jaw opening; jaw deviation to opposite side and protrusion |
| Genioglossus          | Tongue protrusion                                    |
| Hyoglossus            | Tongue protrusion                                    |
| Geniohyoid            | Jaw opening                                           |
| Mylohyoid             | Elevation of hyoid; jaw opening                      |
the muscles involved in oromandibular function and their actions.

As can be seen, any given movement can be produced by several muscles. The masseters, temporalis or internal (medial) pterygoids represent potential injection targets for JCD, and the submental muscles or external (lateral) pterygoids for JOD. Palpation may be helpful in this approach, but not all muscles are palpable. Another approach might be to monitor muscle activity by EMG and inject those muscles that show increased activity during the particular abnormal movement or posture. This is, however, not always possible because EMG recordings of all involved muscles during action dystonia, such as OMD, are technically difficult. In some forms of focal dystonia, the pattern of muscle involvement may change over time (22). Furthermore, dystonia is a disorder of the CNS and specified at the level of movements, not muscles, adding to the complexity of treatment. These issues remain unresolved and studies directly comparing various modes and dosage of BTX administration remain to be done. Thus, different methods of muscle selection, techniques of injection, and assessment of response account for the observed differences across different studies.

RESULTS OF TRIALS OF BTX IN OMD

Many anecdotal and small case series detailing response of OMD to BTX have been reported (23–27), including one using a primary quality-of-life measure (28). We restrict our discussion, however, to the two large case series published. These reports also have the advantage of being relatively recent; i.e., after preliminary experience has allowed refinement of techniques and assessments of results. In the experience reported by the group at Columbia University College of Physicians and Surgeons (CPS), muscle selection was made using EMG and a relatively large number of muscles were considered (29). In the other study, conducted at Baylor College of Medicine (BCM), muscle selection was based on clinical observation and examination coupled with extensive, long-term experience (30). Both groups used BOTOX (Allergan Pharmaceuticals) preparation of BTX type A (BTX-A).

Brin et al. (29) described their experience with 96 patients with OMD. Onset was generally when the patients’ ages were in the mid-40s, but the ages at injection and duration of symptoms are not given. More than 70% of patients in all movement groups had idiopathic OMD. Response was rated primarily by a subjective “linear” scale, in which subjects were asked to assess their percent normal function from 0% to 100%. All muscles involved in jaw motion were considered for injection. EMG was always used to inject the pterygoids and usually to inject the other muscles. In all movement categories, patients’ function improved from about 30% of normal function to about 74% after BTX-A treatment. JDD patients started from a higher baseline (39%) with the same final functional status, and thus showed less percent change; however, only five patients were treated. Adverse effects were seen in 13 of 96 (14%) patients and at 29 of 481 (6%) visits. Of 14 instances of dysphagia, only one was severe enough to require a change in diet. Most of the cases of dysphagia were seen in patients with JOD and were associated with injection of the digastrics. The details of the demographics and response of individual subgroups and muscles are given in Tables 33.3, 33.4, and 33.5. The au-

<table>
<thead>
<tr>
<th>Distribution</th>
<th>BCM</th>
<th>CPS</th>
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<tbody>
<tr>
<td>Jaw-closing dystonia</td>
<td>52.5% (85)</td>
<td>53.1% (51)</td>
</tr>
<tr>
<td>Jaw-opening dystonia</td>
<td>21.6% (35)</td>
<td>41.7% (40)</td>
</tr>
<tr>
<td>Jaw-deviation dystonia</td>
<td>1.9% (3)</td>
<td>5.2% (5)</td>
</tr>
<tr>
<td>Mixed jaw-movement dystonia</td>
<td>24.0% (39)</td>
<td></td>
</tr>
</tbody>
</table>
TABLE 33.4. BTX-A doses in JCD and JOD in case series from Columbia University College of Physicians and Surgeons (CPS) and Baylor College of Medicine (BCM)

<table>
<thead>
<tr>
<th>Muscle</th>
<th>BCM (BOTOX Units)</th>
<th>CPS (BOTOX Units)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Masseter</td>
<td>54.2 (25 to 100)</td>
<td>24.5 (2 to 100)</td>
</tr>
<tr>
<td>Temporalis</td>
<td>—</td>
<td>18.5 (2 to 75)</td>
</tr>
<tr>
<td>Medial pterygoid</td>
<td>—</td>
<td>16.3 (5 to 40)</td>
</tr>
<tr>
<td>Lateral pterygoid</td>
<td>—</td>
<td>15.9 (2.5 to 60)</td>
</tr>
<tr>
<td>Anterior digastric</td>
<td>—</td>
<td>9.8 (3.75 to 30)</td>
</tr>
<tr>
<td>Submentalis</td>
<td>28.6 (10 to 200)</td>
<td>—</td>
</tr>
</tbody>
</table>

Authors do not describe how they verified the placement of the EMG electrode in a particular muscle. For other aspects of the controversy associated with EMG-guided BTX injections, the reader is referred to a recently published review (31).

Tan and Jankovic (30) reported their long-term experience with BTX-A for OMD. Of 202 patients seen from 1988 through 1998, diagnosed clinically to have OMD in a movement disorders clinic over a period of 10 years, 162 patients satisfied the study inclusion criteria of being refractory to other treatments, having at least one follow-up visit and having symptoms of sufficient severity to interfere with swallowing, speech or chewing. The mean age was 57.9 ± 15.3 years and the mean follow-up period was 4.4 ± 3.8 years. The masseters and submental muscles were the only two muscle groups injected with BTX-A for JCD and JOD, respectively, in this group of patients. More than half (52.5%) of the patients had JCD. A total of 2,529 BTX-A treatments were administered into the masseter muscles, submental muscles, or both during a total of 1,213 treatment visits. The mean doses of BTX-A (per side) were 54.2 ± 15.2 U for the masseters and 28.6 ± 16.7 U for the submental muscles. The overall mean total duration of response was 16.4 ± 7.1 weeks. The primary efficacy variable was the global effect of BTX-A. To calculate the global effect score, the “peak effect” (range 0 to 4, where 4 = complete abolition of the dystonia and 0 = no effect) is decreased by 1 if mild adverse effect occurred and by 2 if more severe adverse effect was experienced. The mean global effect of BTX-A was 3.1 ± 1.0. Of the JCD patients, 80% (68 of 85) responded with a score ≥ 3 (i.e., moderate to marked improvement); 40% (14 of 35) of JOD, 33% (1 of 3) of JDD, and 52% (16 of 31) of the mixed patients. Fifty-one (31.5%) patients reported adverse effects with BTX-A in at least one visit. Complications such as dysphagia and dysarthria were reported in 135 (11.1%) of all treatment visits. There was a poorer re-

TABLE 33.5. Therapeutic and adverse effects of BTX-A in JCD and JOD in case series from Columbia University College of Physicians and Surgeons (CPS) and Baylor College of Medicine (BCM)*

<table>
<thead>
<tr>
<th></th>
<th>BCM</th>
<th>CPS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jaw-closing dystonia</td>
<td>80.0</td>
<td>72.0</td>
</tr>
<tr>
<td>Effect (ultimate % normal function)</td>
<td>16.3±8.1</td>
<td>14.6±2.1</td>
</tr>
<tr>
<td>Duration (weeks; mean ± SD)</td>
<td>18.8</td>
<td>11.8</td>
</tr>
<tr>
<td>Adverse events: % of patients</td>
<td>6.2</td>
<td>4.1</td>
</tr>
<tr>
<td>Jaw-opening dystonia</td>
<td>72.5</td>
<td>73.8</td>
</tr>
<tr>
<td>Effect (ultimate % normal function)</td>
<td>16.6±6.9</td>
<td>11.8±2.1</td>
</tr>
<tr>
<td>Duration (weeks; mean ± SD)</td>
<td>40</td>
<td>17.5</td>
</tr>
<tr>
<td>Adverse events: % of patients</td>
<td>15.7</td>
<td>9.9</td>
</tr>
</tbody>
</table>

*A comparison of the two studies is not entirely appropriate because of different methods of patient selection, assessment of results and adverse effects, injection techniques, and other differences.
sponse and higher complication rate with JOD than with the other types of OMD (Tables 33.3–33.5).

Because of different methods of patient and muscle selection, different methods of assessing severity, response, and adverse effects, and different injection techniques, it is impossible to compare the two studies; the overall results, however, appear to be similar. Both studies found that, as compared to JCD, JOD is associated with a higher frequency of adverse effects. While the BCM group reported a longer duration of benefit as compared to the CPS group, there was a higher frequency of adverse effects, probably related to higher dose of BTX-A, higher sensitivity of reporting adverse effects, or both. The higher dose may have been necessitated by greater severity of OMD in the BCM patient population. During the past several years we have modified our technique by directing the injection needle and administering the total dosage as a single bolus into the most anterior portion of the submental complex; this has resulted in a marked reduction in dysphagia and other complications. The CPS group preferentially injects the external pterygoids, and if necessary, adds the digastrics and submentals.

**TONGUE PROTRUSION DYSTONIA**

Tongue protrusion dystonia (TPD) usually interferes with speech and chewing and is most frequently seen in patients with tardive dystonia and with primary (idiopathic) cranial dystonia, but this form of lingual dystonia is also typically present in patients with neuroacanthocytosis. Treatment of this form of focal dystonia is particularly challenging because medications are universally ineffective (except possibly tetra-benzine in tardive lingual dystonia), and BTX-A injections into the tongue muscles can result in severe dysarthria and dysphagia, which are rarely associated with aspiration requiring intubation for airway protection (32).

Gelb et al. reported their experience with 13 patients with TPD (21). They injected an average of 18.3 U (range, 10 to 27) into the genioglossus and hypoglossus muscles, although the exact location of the EMG needle could not be confirmed. The patients’ function improved from 32% to 76% of normal function and the effect lasted 11.2 ± 1.9 weeks. Adverse events were seen in 38.5% of patients and 13% of visits. Five patients developed dysarthria and dysphagia, requiring a change in diet; one developed aspiration pneumonia.

Charles et al. (33) performed a retrospective analysis of clinical findings and results of BTX-A treatment in 9 patients treated at Vanderbilt between 1989 and 1995. After unsuccessful treatment with conventional oral medications the patients were injected with BTX-A into their “genioglossus muscles” at four sites via a submandibular approach. A marked reduction in tongue protrusion was achieved in six patients (67%). Of 35 consecutive injections, 83% were successful at reducing tongue protrusion. Mild dysphagia complicated 14% of the injections. The average dose injected was 34 ± 3 U and the average duration of effect was 15 ± 2 weeks.

Because the various muscles involved in tongue protrusion cannot be reliably differentiated clinically or by EMG sampling, we prefer the term “submental muscles” rather than naming individual muscles layered in the submental area. These muscles are involved in various functions, including tongue protrusion and jaw opening.

**BRUXISM AND OTHER OROMANDIBULAR SYNDROMES**

Bruxism is a diurnal or nocturnal activity that consists of clenching, grinding, bracing, and gnashing of the teeth. Its exact prevalence is unknown, but it is probably much more common than thought because the vast majority of patients with bruxism probably never seek medical attention and the disorder is often misdiagnosed as TMJ (temporomandibular joint) syndrome, although TMJ may occur as a secondary complication of bruxism. Some view bruxism as a form of OMD; it was present in 78.5% of 79 patients with cranial-cervical dystonia (34). Besides dystonia, bruxism can also be seen in a variety of other disorders, particularly mental retardation.
and other forms of CNS damage, as well as neurodegenerative disorders such as Huntington’s disease (35). In an open trial, Tan and Jankovic (36) studied 18 subjects with severe bruxism lasting an average of 14.8 ± 10.0 years (range, 3 to 40). A total of 241 injections of BTX-A were administered in the masseter muscles during 123 treatment visits. The mean dose of the BTX-A was 61.7 ± 11.1 U (range, 25 to 100 U) per masseter muscle on one side. The mean total duration of response was 19.1 ± 17.0 weeks (range, 6 to 78), and the mean peak effect on a scale of 0 to 4, in which 4 is equal to total abolishment of grinding, was 3.4 ± 0.9. Only one subject (5.6%) reported having experienced dysphagia.

OTHER OROMANDIBULAR CONDITIONS

Freund et al. (37) evaluated subjective and objective responses to treatment with BTX-A in an uncontrolled study of a group of 46 patients with various “TMJ” disorders. Both masseter muscles were injected with 50 U each and both temporalis muscles with 25 U each under EMG guidance. Subjects were assessed at 2-week intervals for 8 weeks. Outcome measures included subjective assessment of pain by visual analog scale (VAS), measurement of mean maximum voluntary contraction (MVC), interincisal oral opening, tenderness to palpation, and a functional index based on multiple VAS. There were significant differences in all median outcome measures between the pretreatment assessment and the four follow-up assessments except for MVC. Although MVC was significantly reduced midway through the study, it had returned to pretreatment values by the final two assessments. All other outcome measures remained significantly different from the pretreatment findings. Paired correlation of variables including age, sex, diagnosis, depression index, and time of onset showed no significant differences. BTX-A injections produced significant improvements in pain, function, mouth opening, and tenderness to palpation. MVC initially diminished and then returned to the initial values. Reduced severity of symptoms and improved functional abilities seemed to have extended beyond the period of the muscle-relaxing effects of BTX-A.

A case of recurrent dislocations of the TMJ because of spasticity from multiple sclerosis has been reported (38). This resolved for periods of up to 4 months following chemodenervation of the masseter and pterygoid muscles with injections of BTX-A.

Hemimasticatory spasm is a rare disorder of the trigeminal nerve that produces involuntary jaw closure as a result of unilateral contractions of jaw-closing muscles (39). It is sometimes associated with facial hemiatrophy. The masseter inhibitory reflex is absent during periods of spasm. Needle EMG demonstrates irregular bursts of motor unit potentials that are identical to the pattern observed in hemifacial spasm. The electrophysiologic findings suggest ectopic excitation of the trigeminal motor root or its nucleus, an abnormality that is analogous to ectopic excitation of the facial nerve in hemifacial spasm. This ectopic excitation can be caused by peripheral irritation of the trigeminal nerve itself, entrapment of the motor branches in the infratemporal fossa or focal demyelination of motor branches of the trigeminal nerve. Hemimasticatory spasm has been reported to respond to BTX-A in several case reports (30–42). Masticatory muscle spasms caused by Satoyoshi’s syndrome have also been successfully treated with BTX-A (43).

CONCLUSIONS AND REMAINING QUESTIONS

In summary, BTX-A is now considered the treatment of choice for OMD. Injection into the masseter (and possibly temporalis and internal pterygoids) usually results in marked improvement of JCD and associated bruxism. In JOD, injection of BTX-A into the submental muscles and/or the external pterygoids is usually associated with a robust improvement in jaw opening and dysarthria, although a small percentage of patients may develop transient dysphagia, which can be minimized by directing the injection into the most anterior portion of the submental complex. BTX-A treatment of TPD is also usually
highly successful, although this procedure carries a risk of dysphagia.

There are many unanswered questions that should be addressed by future studies. How do we optimize the therapeutic ratio, especially in JOD and TPD? What is the best method of identifying and selectively injecting the most appropriate muscles? Can additional benefit be obtained by injecting more than one muscle (e.g., injecting temporalis muscles in addition to the maseter muscles in patients with JCD, or injecting pterygoids in addition to submental muscles in patients with JOD)? Because individual muscles in the submental complex are difficult to differentiate by palpation (and even with EMG), what is the role of EMG or ultrasound (44) in locating the muscles responsible for the abnormal jaw movements and postures? What is the role of ethanol and lidocaine (muscle-afferent blockers) (45) in conjunction with BTX-A in the treatment of OMD? Why is dryness of mouth a rare side effect of BTX-A treatment of OMD, but also for a rapidly expanding number of disorders associated with excessive or inappropriate muscle contractions (48).

REFERENCES

16. Giladi N. The mechanism of action of botulinum toxin type A in focal dystonia is most probably through its dual effect on efferent (motor) and afferent pathways at the injected site. J Neurol Sci 1997;152:132–135.