Management of Benign Essential Blepharospasm

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Benign essential blepharospasm (BEB) is a focal dystonia involving the pretarsal, preseptal, and periorbital orbicularis oculi as well as adjacent muscles (Jordan et al. 1989). In this typically bilateral condition, patients experience involuntary contractions of the involved muscle(s). These involuntary spasms can result in decreased quality of life for patients and, in severe cases, can lead to functional blindness. BEB has no known underlying etiology, although it may be associated with increased neural plasticity of the brain. Since its description, numerous treatments have been investigated for this condition. In this chapter, background regarding BEB and its clinical manifestations will be reviewed prior to discussion of various therapeutic modalities.

The earliest recognized documentations of blepharospasm was by the Flemish painter Pieter Brueghel the Elder in the sixteenth century (see Fig. 139.1) in his painting De Gaper. One of the first descriptions of BEB was by the neurologist Henry Meige, who in 1910 identified patients with blepharospasm accompanied by facial muscle spasm as suffering from "spasm facial median." Since that time, it has been recognized that blepharospasm can occur isolated to the orbicularis muscles or, more commonly, along with dystonias of other facial or cervical muscles (Grandas et al. 1988). To this date, "Meige's syndrome" is used to describe those with blepharospasm and concomitant lower facial muscle dystonias. Those with prominent involvement of the mandibular muscles are described as having

Fig. 139.1 Le bâilleur, Yawning Man or De Gaper. Pieter Brueghel the Elder. 1527–1569. Musées Royaux des Beaux-Arts Bruxelles

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M.E. Hartstein et al. (eds.), *Pearls and Pitfalls in Cosmetic Oculoplastic Surgery*,
DOI 10.1007/978-1-4939-1544-6_139,

"Brueghel's syndrome" or "oromandibular dystonia" (Marsden 1976). Nearly half of patients with Brueghel's syndrome have been found to exhibit more generalized dystonia with involvement of respiratory and truncal muscles (Marsden 1976). Meanwhile, the term BEB is typically reserved to describe patients with only periocular dystonias. If the process extends to the distribution of other cranial nerves, it has been described as segmental cranial dystonia or craniocervical dystonia (Tolosa 1981).

Epidemiology

The prevalence of focal dystonias in the population lies between approximately 2 and 7,000 patients per million (Defazio et al. 2004; Duffey et al. 1998; Müller et al. 2002a; Nakashima et al. 1995; Nutt et al. 1988; Warner et al. 2000); the wide variation in these numbers may be due to diagnostic bias or ethnic/regional variations in prevalence. When looking at BEB alone, prevalence varies between approximately 16 and 133 patients per million (Defazio and Livrea 2002). There is an approximately 3:1 female-to-male ratio, and most patients experience onset of symptoms in the 40s and 50s (Grandas et al. 1988; Nutt et al. 1988). Female gender, age, family history of dystonia/postural tremor, personal history of facial and/or head trauma, and personal history of ocular disease have been linked to development of BEB (Hallett et al. 2008). No particular gene has been implicated in BEB although family history does appear to be a risk factor. Some studies have suggested a polygenic inheritance versus autosomal dominant inheritance with low penetrance (Hallett et al. 2008; Defazio et al. 2008). The disorder has also been correlated with Type A personality.

Clinical Manifestations

The hallmark sign of BEB is uncontrolled eyelid closure due to spasm of related muscles. The first manifestation of BEB is often increased blink rate, which then advances to the full disease. If spasm is severe, patients are rendered functionally blind. In addition to spasms and decreased vision, patients may complain of photophobia. The pathophysiology of photophobia seen in BEB has not been elucidated but may be related to the trigeminal pathway, occipital lobe, and/or thalamus. Patients can also be confronted with complications of long-term muscle contractures, such as brow ptosis, dermatochalasis, and lateral canthal tendon deformities (Gillum and Anderson 1981) (see Table 139.1).

Table 139.1 Common clinical manifestations seen in BEB (Grandas et al. 1988; Anderson et al. 1998)

Clinical manifestation	Rate (%)
Increased blinking	77
Eyelid spasm	66
Mid-facial or lower facial spasm	59
Eye irritation/dry eye	55
Photophobia	25
Brow spasm	24
Eyelid tic	22
Tearing	2
Blepharitis	1.5
Ocular pain	<1

Conditions to be considered in the differential diagnosis of BEB include: reflex blepharospasm, Meige's syndrome, tardive dyskinesia, hemifacial spasm, ocular disease (i.e., ocular surface disease), Parkinson's disease, brainstem disease, medication side effect, habit spasms, facial tics, seizure, encephalitis, and functional blepharospasm (Jankovic 1982). The pathophysiologic basis of BEB remains unclear. A neurologic etiology such as disease of the motor cortex or basal ganglia has been postulated (Marsden 1976; Jankovic 1982; Henderson 1956). Alterations in blinking in patients with dopaminergic diseases suggest a link to this neurotransmitter. As of yet, however, no clear association with any of the above has been established.

BEB is typically a lifelong disease; however, one retrospective study of 238 patients with BEB and Meige's syndrome showed 11.3 % patients experienced remission without treatment (Castelbuono and Miller 1998). If it did occur, remission was most often seen within the first 5 years of diagnosis and lasted on average

6.33 years. Triggers identified for blepharospasm include: bright light, stress, wind, smoke, fatigue, driving, and reading. Intense concentration and/or tasks involving the use of the facial nerve have been noted to decrease symptoms. These are called sensory tricks. For example, patients have identified improvement in symptoms with activities such as humming, yawning, chewing gum, talking, and completing tasks requiring concentration (Henderson 1956).

Treatment: Oral Medications

Numerous medications have been tried in the treatment of BEB (see Table 139.2). Because the pathophysiologic basis of BEB remains unclear, many treatments have been empirically employed in this disorder. Despite some successes, it has been difficult to find drug classes that consistently improve BEB symptoms. Dopamine has been suggested as a player in the development of blepharospasm; as such, dopamine antagonists, such as tetrabenazine and haloperidol, have been found to improve symptoms in some patients with Meige's syndrome (Jankovic 1982; Jankovic and Ford 1983). Interestingly, dopamine agonists such as levodopa have also been shown to improve BEB symptoms (Cohen et al. 1986). Cholinergics have also been investigated. Paradoxically, both cholinergics and anticholinergics have been found to be helpful in this disease (Grandas et al. 1988). Benzodiazepines such as clonazepam have been shown to be useful in symptom management, perhaps due to effects on serotonin. Other drugs that have been found to be useful include: lithium, antipsychotics (such as phenothiazine), sedatives (such as phenobarbital), and muscle relaxants (such as baclofen and diazepam) (see Table 139.2). Sedatives and muscle relaxants have been less preferred due to their lack of specificity to the ocular muscles and thereby propensity for global sedation/muscular reaction.

Grandas and colleagues studied 264 patients who received various treatments for blepharospasm (Grandas et al. 1988). In this study, approximately 20 % of patients treated medically responded with decrease in their symptomatology. Unfortunately, these effects were often not lasting, causing patients to require further management. A limitation of this study is that 14 % of study patients had underlying conditions potentially contributing to their blepharospasm, such as Parkinson's disease or tardive dyskinesia. These associations could explain some of the response to medical therapy (i.e., dopaminergic drugs in Parkinson's patients).

As discussed below, botulinum neurotoxin therapy is common among BEB patients. Another approach to oral therapy is the development of adjunctive treatments to botulinum toxin. Because botulinum toxins require zinc for functioning, one study looked at the influence of

Table 139.2 Overview of oral medications for the treatment of blepharospasm, as reported in the literature

Medications	
Class	Drug(s)
Dopamine antagonists	Tetrabenazine, haloperidol, pimozide, chlorpromazine
Dopamine agonists	Levodopa, bromocriptine, lisuride
Cholinergic agents	Deanol, choline chloride
Anticholinergic agents	Trihexyphenidyl, benztropine, biperiden, atropine, procyclidine, orphenadrine, scopolamine, and ethopropazine
Benzodiazepines	Clonazepam, lorazepam, diazepam
Lithium salts	Lithium carbonate
Antipsychotics	Phenothiazine
Sedatives	Phenobarbital
Muscle relaxants	Baclofen, cyclobenzaprine
Stimulants	Methylphenidate, amphetamine
Ocular lubricants	Artificial tears
Antianxiety	Meprobamate
Selective serotonin reuptake inhibitor	Sertraline
Adjuncts to injectable medications	Zinc, phytase
Antihistamines	Diphenhydramine

As discussed above, few have shown to be reliable and effective treatment options for the general BEB population

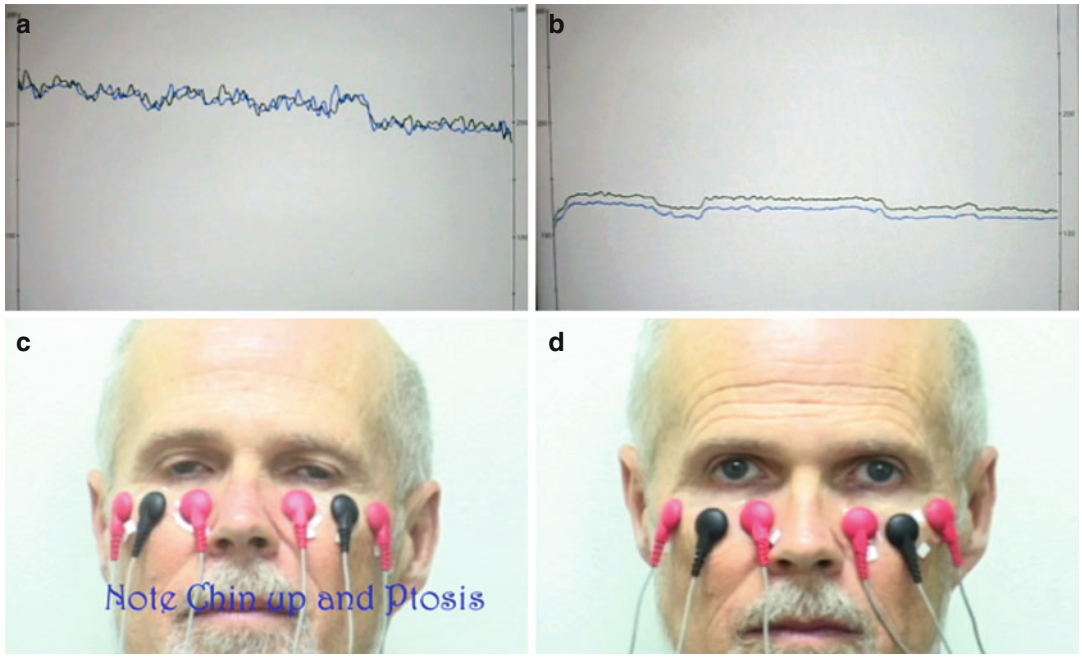

Fig. 139.2 Effects of methylphenidate treatment on patient with BEB. (**a**) EMG recording prior to methylphenidate dosing. (**b**) EMG recording several minutes after dose given. (**c**) Patient prior to methylphenidate. (**d**) Patient several minutes after dose given

zinc and phytase (increases zinc absorption) supplements on response to botulinum toxin treatments (Koshy et al. 2012). The data suggested that zinc and/or phytase may augment the amount of response seen from treatment with botulinum toxin. However, in this study, 50 mg of zinc with phytase was compared to zinc alone, suggesting the need for more equally controlled studies in the future to clearly discern the effects of these supplements on BEB treatment.

Methylphenidate's effects on blepharospasm have been investigated in seven patients already using methylphenidate for other indications. Spasms were improved both on video recordings and EMG (see Fig. 139.2). These patients were found to have lower mean voltage on sEMG potential after methylphenidate dosing (50 % decrease in the right eyes, 31 % decrease in the left eyes). Functional disability scores were significantly lower after methylphenidate administration as well ($p = 0.016$). For treatment, this can be prescribed as methylphenidate 20 mg every morning or 10 mg twice daily. These promising results suggest that further study of methylphenidate use in blepharospasm patients would be of interest.

Treatment: Injectable Medications

Injection with botulinum toxin is generally considered the first-line treatment for BEB. It is important to note when starting patients on botulinum toxin injections that many insurance companies require an oral medication trial to be documented first. There are seven distinct serotypes of neurotoxin produced by *Clostridium botulinum*, a soil-dwelling gram-positive anaerobic bacterium (see Table 139.3). These toxins alter calcium ion metabolism at the neuromuscular junction thereby blocking the release of presynaptic acetylcholine. The release of presynaptic acetylcholine is reliant upon the activity of the SNARE complex of proteins. Different serotypes of botulinum toxin cleave various SNARE proteins (i.e., botulinum toxin A cleaves SNAP-25), resulting in the block of acetylcholine release. This results in paralysis of the muscle. The botu-

Table 139.3 Overview of available botulinum neurotoxins for the treatment of BEB and related dystonias (Allergan 2013; Ipsen Biopharmaceuticals and Medicis Aesthetics 2012; Merz Pharmaceuticals 2010; Solstice Neurosciences 2011)

Drug name (Serotype)	FDA approval	On-label usage	Vial size	Composition	Molecular weight	Storage (packaged; reconstituted)	FDA-approved dosage	On-label preparation	Frequent off-label preparations	Protein cleaved (mode of action)
OnabotulinumtoxinA (A)	2002	Blepharospasm associated with dystonia in patients ≥12 years Urinary incontinence Migraine prophylaxis Upper limb spasticity Cervical dystonia Severe axillary hyperhidrosis Strabismus	50 U, 100 U	*C. botulinum* toxin type A ATCC 3502 (Hall strain) hemagglutinin complex	900 kDa	2–8 °C or <–5 °C	1.25 U–2.5 U per each of 3 sites per eye	Dispensed as powder; reconstitution with 2.5 mL of preservative-free saline using one vial for one patient only	Preserved saline 1.0–4.0 mL diluent Store for 7–10 days after reconstitution Multiple patients per vial	SNAP-25
AbobotulinumtoxinA (A)	2009	NOT approved for functional use	300 U	*C. botulinum* toxin type A ATCC 3502 (Hall strain) hemagglutinin complex	500–900 kDa	2–8 °C	N/A	N/A	N/A	SNAP-25

(continued)

Table 139.3 (continued)

Drug name (Serotype)	FDA approval	On-label usage	Vial size	Composition	Molecular weight	Storage (packaged; reconstituted)	FDA-approved dosage	On-label preparation	Frequent off-label preparations	Protein cleaved (mode of action)
IncobotulinumtoxinA (A)	2011	Blepharospasm in patients already treated with onabotulinumtoxinA Cervical dystonia	50 U, 100 U	*C. botulinum* toxin type A ATCC 3502 (Hall strain)	150 kDa	Up to 25 °C	Same as prior dose of onabotulinumtoxinA or 1.25 U–2.5 U per each of 3 sites per eye if prior dose is unknown	Dispensed as powder; reconstitution with 0.5–8.0 mL of preservative-free saline using one vial for one patient only	See above	SNAP-25
RimabotulinumtoxinB (B)	2000	Cervical dystonia	2,500 U, 5,000 U, 10,000 U	*C. botulinum toxin* type B in association with hemagglutinin and nonhemagglutinin proteins	700 KDa	2–8 °C (no freezing)	2,500–5,000 Units divided among affected muscles if prior botulinum toxin treatment; start at lower doses if no prior treatment	Comes as prepared solution (0.5 mL, 1 mL, 2 mL)	Multiple patients per vial	VAMP

Comments: Contraindications similar for all preparations: hypersensitivity to product, infection at injection site, pregnancy, breast feeding, diseases of neuromuscular junction (i.e., myasthenia gravis, Eaton-Lambert), autoimmune disorders, and drug interactions (aminoglycosides, cyclosporine, calcium channel blockers, cholinesterase inhibitors)

linum toxin complex is between 300 and 900 kDa in size depending on the serotype; this includes the neurotoxin itself, which is 150 kDa, and complexed proteins that surround the toxin. The neurotoxin must be cleaved into a 50 kDa light chain and 100 kDa heavy chain for activity. Scott initiated the use of botulinum toxin in ophthalmology, utilizing it initially in the treatment of strabismus (Scott 1980; Scott et al. 1973). Within years, its use was broadened to include blepharospasm (Scott et al. 1985).

There are few controlled trials establishing botulinum toxin injection as the treatment of choice for BEB. In one trial of eight patients (Fahn et al. 1985), patients receiving botulinum toxin experienced fewer contractions at rest (78.6 vs 51.4), fewer maximally forced contractions (663 vs 338), and lower muscle potential (2.08 mV vs 0.95 mV). In another trial of 12 patients, a 72 % improvement in the severity of symptoms was noted in those receiving botulinum toxin (Jankovic and Orman 1987). Those receiving placebo did not note any significant improvement. Symptomatic improvement was noted 3.7 days postinjection for approximately 12.5 weeks. Although a small trial, this study along with other noncontrolled trial data helped form the basis for the eventual FDA approval of botulinum toxin for BEB treatment. Despite the dearth of randomized, controlled studies, there are a number of case series and other studies reporting botulinum toxin as an effective and safe, albeit transient, treatment for BEB. Review of the literature reveals approximately 75–100 % of patients experience symptomatic benefit from botulinum toxin therapy (Costa et al. 2005; Dutton 1996). Effects have been seen to last approximately 3 months (Dutton and Buckley 1988; Shorr et al. 1985). Overall, reports show an average onset of symptomatic relief at 1–14 days lasting for 3–4 months (Dutton and Fowler 2007). With the current strength of evidence in support of botulinum toxin therapy, it has been argued that the pursuit of further randomized, controlled trials would be unethical.

IncobotulinumtoxinA, the most common formulation of botulinum toxin, comes packaged in 50-unit and 100-unit vials (see Table 139.3). These are recommended for storage at 36–46 °F for 36 months. For reconstitution, 2.5 mL of preservative-free saline is used with only a gentle rotation of the bottle to ensure suspension (more aggressive mixing may damage the toxin). The typical first-time dosage is 1.25 units to 2.5 units per each of 3 injection sites per eye (see Fig. 139.3). Clinical experience dictates preserved saline can also be used successfully. As well, reconstituted onabotulinumtoxinA has been known to work for up to 7–10 days, although FDA approval is only for use up to 24 h after reconstitution. Although FDA approval is for use with only one patient per vial, there is often sufficient medication available for use on multiple patients per vial if sterile technique is used to draw up medication safely. AbobotulinumtoxinA is available for cosmetic use but does not have FDA approval for functional use such as that for BEB; this drug will not be discussed further in this chapter. IncobotulinumtoxinA, discussed further below, provides another treatment alternative. Reconstitution is similar to that of onabotulinumtoxinA, and initial dosing is recommended at the patient's usual onabotulinumtoxinA dose. IncobotulinumtoxinA may be preferable in warmer climates as it can tolerate storage at temperatures of 68–77 °F for up to 36 months; after reconstitution, however, it is recommended for storage similar to onabotulinumtoxinA. Following reconstitution, medication is injected using a 27-gauge needle just under the skin into the orbicularis muscle in the injection pattern seen in Fig. 139.3.

Contraindications to treatment include allergy/sensitivity to the drug, infection at the injection site, and neuromuscular junction disease such as myasthenia gravis or Eaton Lambert. Pregnant women should avoid botulinum toxin as animal data show potential adverse effects to the fetus. Complications from botulinum toxin injection are seen in approximately 20 % of injections (Cohen et al. 1986; Dutton and Buckley 1988). The common side effects of botulinum toxin injection include ptosis (less than 10 %), diplopia (less than 1 %), dry eye (less than 10 %), photophobia (<5 %), and local lid edema/irritation. Dry eye symptoms may be related to corneal

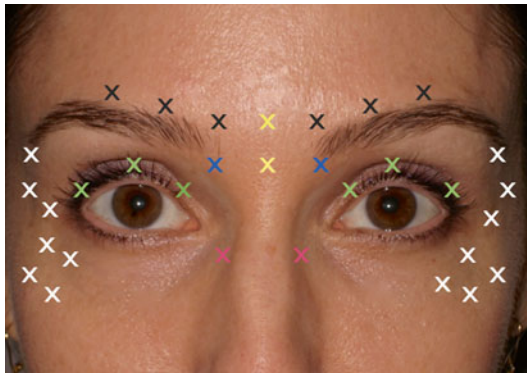

Fig. 139.3 Suggested injection sites for botulinum toxin for patients with BEB. Muscles involved include: *black*, corrugator supercilii; *yellow*, procerus; *blue*, depressor supercilii; *green*, pretarsal orbicularis; *pink*, upper nasalis; and *white*, lateral orbicularis oculi

Table 139.4 Common complications reported after treatment with onabotulinumtoxinA (Cohen et al. 1986; Dutton and Buckley 1988)

Complication	Approximate frequency
Ptosis	10–15 %
Diplopia	<1–4 %
Dry eye/irritation	3–10 %
Tearing	4 %
Local lid swelling	2 %
Photophobia	2–3 %
Facial weakness	1 %
Ectropion/entropion	<1 %
Ecchymosis	<1 %
Pain	<1 %
Blurry vision	<1 %
Numbness	<1 %
Difficulty breathing, swallowing, or speaking	Rare, due to systemic effect

exposure due to decreased blink rate following toxin administration. Although uncommon, there is potential for distant spread of botulinum toxin following injection, causing systemic effects such as respiratory distress and/or difficulty swallowing. This can be seen hours to weeks after injection and, in some very rare cases, may lead to death (Table 139.4).

Various methods of botulinum toxin injection have been studied. Injection into the pretarsal orbicularis oculi has been shown to have a response in a larger proportion of patients for a longer time interval with fewer side effects (Albanese et al. 1996; Çakmur et al. 2002; Jankovic 1996; Kowal and Albanese 1997). In a randomized, double-blind study, Frueh and colleagues found no difference in patients receiving botulinum toxin versus saline injections to the lower lid when receiving standard treatment to the upper lids and brow (Frueh et al. 1988). Because of this result, the authors advocated excluding the lower lid in treatment in hopes of decreasing side effects such as diplopia and ectropion secondary to inferior oblique involvement. Clinically, many practitioners have avoided the central upper lid on injections due to theoretical risk of ptosis. In our experience with botulinum toxin injection including the central upper lid in 13 patients over 10 years, ptosis was rare with an incidence of only 0.77–1.2 %. Because of these results, it may be advisable to include treatment of the central upper lid with botulinum toxin injections for improved relief from blepharospasm without increased risk of induced ptosis. Instead, ptosis may be more likely due to injections given too deeply, causing medication to track along the periosteum in the corrugators (Ramey and Woodward 2010).

Another form of botulinum toxin, rimabotulinumtoxinB is available but only FDA approved for cervical dystonia and not for BEB. Reports have shown that this type B toxin can be useful in patients who have decreased response to botulinum toxin A. The mechanism of this increased effectiveness in this special patient population may be due to antibody formation to botulinum toxin A. Suggested dosing for type B toxin is 50–100 times the patient's prior dose using botulinum toxin A. The duration of effect of botulinum toxin B is shorter than that of toxin A at 8–10 weeks and can be more uncomfortable on injection because of its acidic pH. For these reasons, the use of botulinum toxin B would not be recommended as a first-line treatment (Dutton 1996).

Prior to treatment with injectable botulinum toxin, it is important to evaluate patients for concomitant conditions. Some patients with blepharospasm may also suffer from apraxia of

lid opening. In this condition, patients have deficits in levator contraction, leading to eyelid closure. Studies using electromyography (EMG) have demonstrated a spectrum of involvement of the orbicularis oculi muscles and the levator muscles in those who have been clinically diagnosed with blepharospasm (Aramideh et al. 1994a, b; Hallett 2002). Those with isolated involvement of the orbicularis show the best response to botulinum toxin injections with progressively decreased response in those who have levator involvement. Injecting in multiple locations in the orbicularis as well as injection into the pretarsal orbicularis may increase effect in these more difficult-to-treat patients (Çakmur et al. 2002). It may be reasonable to utilize EMG in those patients diagnosed with BEB who do not respond well to botulinum toxin injections.

If patients lack response to botulinum toxin, attention must be paid to the method of administration and concomitant conditions as discussed above. Such patients may benefit from combined treatment with surgery such as suspension of the frontalis or excision of the pretarsal orbicularis oculi. It has been posited that patients can develop antibodies to botulinum toxins decreasing their effectivity; however, studies have shown benefits persist after multiple injections (Dutton and Buckley 1988; Jankovic and Schwartz 1993).

The Battle of the Neurotoxins

Traditionally, onabotulinumtoxinA was used for treatment of BEB as it was the first formulation of botulinum toxin. OnabotulinumtoxinA is a 900 kDa compound made up of a 150 kDa core neurotoxin complexed with proteins (see Fig. 139.4). The purpose of this complex of proteins is likely to guard the neurotoxin from degradation in the acidic GI tract. By this logic, incobotulinumtoxinA has more recently been formulated as a "pure" neurotoxin without complexing proteins; the thought being that extra complexing proteins bind T cells and trigger cytokine cascades that are unnecessary. Allergan's argument is that incobotulinumtoxinA needs approximately twice as much human serum albumin to prevent molecules from sticking to the medication vial. IncobotulinumtoxinA was compared to onabotulinumtoxinA in a randomized, double-blind study treating 300 blepharospasm patients; no significant difference was found in efficacy or adverse effects (Roggenkämper et al. 2006; Wabbels et al. 2011). Meta-analysis to determine appropriate dosage of the two toxin formulations resulted in a recommendation to use equivalent doses between onabotulinumtoxinA and incobotulinumtoxinA (Jandhyala 2012). Furthermore, no significant subjective preference between the two drugs has been established (Chundury et al. 2013). An additional formulation,

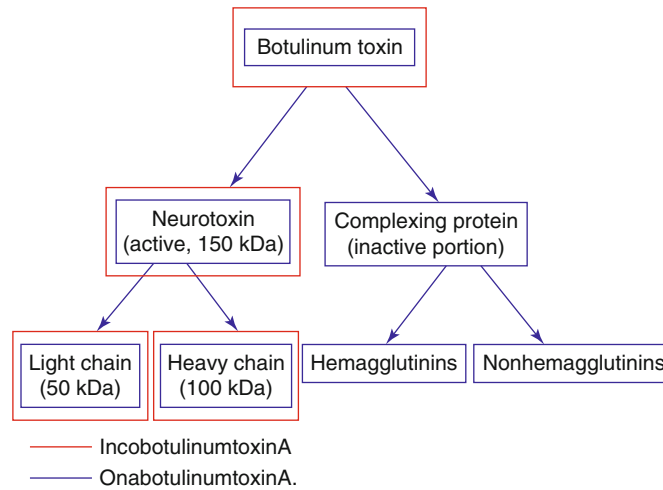

Fig. 139.4 Botulinum toxin (onabotulinumtoxinA vs incobotulinumtoxinA) and association with complexing proteins. Note, there are no complexing proteins seen with incobotulinumtoxinA

abobotulinumtoxinA, is also available (see Table 139.3). Currently, this formulation is only FDA approved for cosmetic indications and will not be discussed further in this chapter.

Although botulinum toxin injections are the most prevalent injectable treatment for BEB, other injections have been used. In hopes of more lasting effect, chemical myectomy using doxorubicin has been investigated. In some patients, this has provided years of symptomatic improvement. However, severe adverse effects, including local skin necrosis, have made this a less acceptable treatment option than botulinum toxin. Limited studies of liposome-encapsulated doxorubicin have shown promise for less local skin involvement, but this remains a less used treatment (McLoon and Wirtschafter 2001). Chemical myectomy with ricin has also been postulated and tried in animal studies but has not been widely adopted for human use. Blockade of the superior sympathetic ganglion with local anesthetic has been studied for symptomatic improvement in patients with associated photophobia. The theoretical basis behind this treatment is the proposed relationship between sympathetic pathways and photophobia. In one study, 13 of 19 patients stated that symptoms were improved with the above blockade and eyelid spasm decreased (McCann et al. 1999).

Surgical Management

For those patients for whom medical therapies are insufficient, surgical management may be required. Surgical interventions predate the current first-line injectable treatments. Surgical disruption of the facial nerve has been used in the treatment of facial dystonias since the 1920s (Cohen et al. 1986). In the 1960s, Reynolds and colleagues advocated selective peripheral facial nerve avulsion (Reynolds et al. 1967). Although this is capable of relieving eyelid spasms, results were often undesirable as patients were left with bilateral facial palsy. Patients also suffered from adverse effects such as ptosis, lagophthalmos, ectropion, and facial droop. Recurrence rates with this procedure were also relatively high: 35–50 % after 15 months and 50–55 % after 2 years (Callahan 1965). Because of the functional deficits following surgery as well as the high recurrence rate, facial nerve avulsion is rarely used today.

In the 1980s, Anderson and colleagues advocated the full myectomy procedure to weaken eyelid protractors while increasing the power of retractors (Gillum and Anderson 1981). This involves removal of the orbicularis oculi and corrugator superciliaris muscles as well as tightening of the levator aponeurosis. If there is lid apraxia, the procedure can be combined with frontalis suspension. For full myectomy, browplasty incisions are made with the greater elevation on the lateral aspect of the brow. Underlying tissue is excised down to the galea sparing the medial neurovascular bundle. Care is taken to excise the orbital orbicularis inferiorly and then the corrugator superciliaris nearly to the medial canthal tendon. The procerus muscle is then excised between the brows. The deep tissue layer is then closed while attaching the frontalis muscle to the deep tissues. Subcutaneous tissue is then closed. Blepharoplasty incision is then made, and the underlying tissue is removed from the eyelid including the preseptal and pretarsal orbicularis and postorbicular fascia. Of these tissues, only a small portion of the pretarsal orbicularis is spared to preserve the follicles. The area is then reapproximated and closed, attaching the levator aponeurosis to the tarsus. Myectomy results in a significantly lower need for repeat surgical intervention (approximately 20 %) versus facial neurectomy (McCord et al. 1984). Partial myectomy can be done for a less aggressive approach as described below.

Pearls for the Partial Laser Surgical Myectomy

In order to avoid the unsightly scars from a full myectomy, but still provide an aesthetically pleasing operation, a partial myectomy with the CO_2 laser can be performed swiftly and elegantly (see Fig. 139.5). This CO_2 laser provides excellent hemostasis so that a more clear view of the

Fig. 139.5 Critical steps during limited myectomy. *Top*: removal of the pretarsal orbicularis. *Middle*: subsequent removal of the lateral orbicularis. *Bottom*: careful dissection of the lateral nerves is important to the success of the procedure

relevant anatomy is possible. It is faster than a blade not only because of this hemostasis but because the laser tip has many functions including cautery, dissection, and cutting therefore limiting the need to switch between various instruments. Most lasers have a 0.2 mm focused delivery system. This size or smaller is desirable. Proper laser precautions such as protective eyewear, no supplemental oxygen, laser safe drapes, and a sign on the door must be followed.

Marking the patient is similar to a standard blepharoplasty except that slightly less skin is removed because there is more scar tissue and contraction after the procedure, and so this will give a little leeway to assure closure of the eyelids.

As the globe is protected with a metal shield, the laser is set at 6 W in continuous wave in order to make the skin and muscle incisions. The laser is drawn slightly slower than with a standard blepharoplasty to ensure penetration into the orbicularis. The flap is then elevated and the laser is defocused at 1 cm to remove the skin and muscle in a side-to-side fashion against a wet gauze.

Next, the pretarsal skin is dissected away from the pretarsal orbicularis. Care is taken to approach the follicles but not disturb them with the laser to avoid madarosis. Careful dissection is also important to avoid perforation of the skin. The pretarsal muscle is then elevated with a forceps laterally as the laser is used to remove it from across the tarsus. Removal of the muscle along the far lateral tarsal plate is important because this carries branches of the facial nerve for eyelid closure, and thus removal of these will minimize the patient's spasms. This can also be accomplished by using the laser in a 3–4 cm defocused mode to destroy the muscle with thermocoagulation.

Next, the laser is used to dissect the skin away from the orbicularis in a 1–2 cm radius from the tail of the blepharoplasty incision. This muscle is then pulled up so that it can be removed with the laser. This same technique is used to remove the orbicularis superior and medial to the blepharoplasty incisions. A levator advancement can also be performed at this time since many blepharospasm patients are in need of this as well. Lastly, the incision is then closed in a standard manner. Healing may involve more postoperative edema than with a standard blepharoplasty. Patients will need reassurance and perhaps a short course of oral steroids to minimize edema. Figure 139.6 shows a patient pre and 6 weeks post laser myectomy.

In the authors' experience, over 80 % of patients noticed marked improvement of their spasms and were able to decrease their use of oral medications and injectable neurotoxins. After

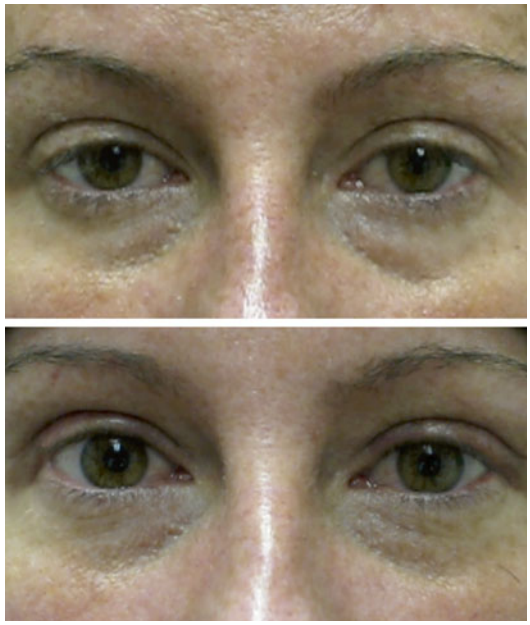

Fig. 139.6 Demonstrates a patient pre-op and 6 weeks post-op laser partial myectomy. Note her MRD has improved and she still carries some edema

years of time, the patients may slowly increase their use of these therapies again because the disease itself experiences progression; however, the patients will report that they are still better off than prior to the myectomy.

Deep brain stimulation is a developing surgical advancement in the treatment of recalcitrant BEB. Treatment is given to the globus pallidus internus. Similar treatment has been effective in the treatment of more generalized dystonias, but successful treatment of facial dystonias has proven to be more difficult. Preliminary case reports and series show promising results with up to 75 % improvement posttreatment (Foote et al. 2005; Ostrem et al. 2007). A multicenter case series of 12 patients with Meige's syndrome found 45 % improvement at 4 months and 53 % improvement at 3 years post-deep brain stimulation (Reese et al. 2011).

Transcranial magnetic stimulation has also shown promise as a less invasive medication-sparing therapy for BEB (Abbruzzese et al. 2001; Kranz et al. 2010). In one study of 12 BEB patients, 15 min of transcranial magnetic stimulation of the anterior cingulate cortex (thought to be implicated in BEB) resulted in decreased blink rate, decrease in the number of spasms recorded by physicians, and decrease in number of spasms noted by patients directly following the procedure. In the future, this may be a promising treatment sparing patients from oral and injectable medications as well as more invasive surgical maneuvers.

Prognosis

As reviewed above, advances in treatments for BEB have allowed patients with this condition to live with fewer symptoms. Control of BEB allows greater visual function and spares patients other sequelae of long-term muscle spasm, such as dermatochalasis. Additionally, numerous studies have shown patients with BEB suffer from decreased quality of life and psychiatric comorbidities, such as depression. One study identified up to 40 % of BEB patients as suffering from depression (Müller et al. 2002b; Wenzel et al. 2000). Fortunately, those undergoing treatment with botulinum toxin have shown improvement in quality of life (MacAndie and Kemp 2004). In addition to those treatments discussed above, patients may enjoy improvement in symptoms and quality of life through the use of sunglasses, better dry eye control with punctual plugs, biofeedback exercises, acupuncture, or relaxation.

Future Directions

Despite the advances made in treatment of BEB in the past several decades, we continue to lack a long-term treatment with few side effects. Botulinum toxin has been beneficial to many patients, but its effects remain transient, leaving patients to endure repeat treatments every 3 months. Current surgical treatments can provide more lasting relief but are more invasive and can be plagued by adverse events. In the future, longer-acting drugs and less invasive surgical techniques would be a boon to tomorrow's BEB patients.

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