

## Oculofacial Diagnosis and Management of Benign Essential Blepharospasm

**B**lepharospasm is a facial dystonia characterized by involuntary contraction of the orbicularis oculi and other muscles involved in eyelid closure, including the procerus and corrugator. Blepharospasm can range from sporadic and mildly irritating to functionally blinding. The most common type of this disorder is benign essential blepharospasm (BEB, Fig. 1), which is the primary focus of this article. In Meige syndrome, a less common variant, blepharospasm and oromandibular dystonia occur together. Blepharospasm can also be associated with systemic disorders such as Parkinson disease or other common ocular conditions such as blepharitis or dry eye.

### Epidemiology

BEB has a prevalence of approximately 4.2 cases per 100,000 people.<sup>1</sup> It commonly presents in the fifth to seventh decades of life. There is a female predominance, with a female-to-male ratio estimated as 2:1 to 4:1. Menopause may be a predisposing factor.<sup>2</sup> Coffee consumption may have a protective effect against BEB.<sup>3</sup>

### Pathophysiology

The pathophysiology of BEB is poorly understood but may be localized to the basal ganglia that play an important role in the coordination of eyelid movements. In one study, lesions in the basal

ganglia, thalamus, midbrain, and cortex were identified in some patients with BEB.<sup>4</sup> Imbalance in neurotransmitters, namely dopaminergic inhibition, a decreased function in gamma-aminobutyric acid (GABA), and cholinergic hyperactivity, are thought to cause the muscle hyperactivity. This neurotransmitter imbalance may also be the basis for the anxiety and depression that can accompany BEB.

### Clinical Presentation

The primary and most common form of blepharospasm, BEB, often presents initially as infrequent bilateral eyelid twitching that may progress over time to forceful and frequent spasms of the eyelid closure muscles. Bilateral, synchronous, and stereotyped eyelid contractions, with or without twitching of other facial muscles, may be observed. It may also lead to eyelid apraxia, a transient inability to voluntarily open the eyes.

Some patients report triggering factors such as headlights in oncoming traffic while driving or other bright lights. Photosensitivity is a common sensory complaint in patients with BEB, with up to 79% reporting this symptom.<sup>5</sup> The eyelid spasms abate

during sleep. Many patients also report that sensory stimulation, such as touching the eyelids or singing, can result in temporary cessation or reduction of the contractions.

Blepharospasm may be accompanied by other disorders. For example, the slit-lamp exam may reveal signs of blepharitis and ocular surface disease. Approximately 30% to 60% of patients with blepharospasm report concurrent anxiety or depression.<sup>6</sup> When blepharospasm is part of Meige syndrome, it is associated with facial grimacing. Patients may also have an increased blink rate at baseline and while speaking.

### Diagnosis

BEB is a diagnosis of exclusion based on clinical assessment. Imaging or laboratory studies are usually not indicated and have no utility in confirming



**PHASES OF BEB.** These images depict the contractions of eyelid closure muscles in BEB.

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the diagnosis. Although electromyography can objectively characterize the muscle involvement, the test is rarely performed in clinical practice.<sup>7</sup>

**Differential diagnosis.** The differential for blepharospasm includes Meige syndrome, myokymia, apraxia of eyelid opening, hemifacial spasm, tardive dyskinesia, and tic disorders (e.g., Tourette syndrome). Conditions that cause photophobia, such as anterior uveitis or ocular surface disease, can incite regular eyelid contractions that may be confused with BEB. Of note, if the periocular spasms improve after application of anesthetic drops, ocular surface irritation is a more likely diagnosis than BEB.

Meningeal irritation or infection are other rare causes of photophobia, which can incite periocular spasms. Psychogenic facial spasms should also be considered in the differential, especially in younger patients (25-40 years old) who have experienced recent emotionally traumatic events.

The symmetry, distribution, and accompanying symptoms can help to differentiate among these conditions. For example, myokymia is typically unilateral, and the eyelids exhibit asynchronous spasms. It must be distinguished from hemifacial spasm, which is characterized by involuntary tonic/clonic contractions involving the whole of one side of the face; this condition is sometimes caused by compression of the facial nerve by a blood vessel or tumor.

## Management

No cure has yet been found for BEB. For the past 30 years, botulinum neurotoxin (types A and B) injections have been the mainstay treatment. Other adjunctive treatments may occasionally be helpful. Surgical treatment is reserved for medically resistant cases.

**Photochromatic modulation.** Many BEB patients are photosensitive, so spectacle lenses with an FL-41 tint may be helpful, even in low light. Superior cervical ganglion blocks have been shown to provide relief for the photophobia in some patients with BEB.<sup>8</sup>

**Botulinum toxin.** The first-line and most common treatment for BEB is

botulinum neurotoxin injections every three to four months to the eyelid closure or brow depressor muscles. This treatment can be administered as soon as the diagnosis is made. Doing so can help slow disease progression.

Botulinum toxin injections have some risks, including ptosis, dry eye, ecchymosis, diplopia, epiphora, photophobia, and ectropion. The most common of these are ptosis and dry eye, occurring in roughly 7% of treated patients.<sup>9</sup>

Good administration technique is the best defense against these side effects. Using an insulin-type syringe, botulinum toxin should be administered submuscularly into the lateral and medial aspects of the upper eyelid, inferior glabellar, and procerus muscles. Typically, each site should receive .1 cc or less of the drug during the first treatment to avoid diffusion to nearby musculature. Care should be taken to avoid injecting the central upper eyelid to minimize affecting the levator palpebrae and causing ptosis. The medial lower eyelid should also be avoided to prevent lacrimal complications due to ectropion of the puncta. To minimize the risk of complications, some clinicians inject the orbicularis oculi muscle subcutaneously. Immediately afterward, small wheals appear at the injection sites.<sup>9</sup>

Over the long term, some patients require a shorter interval between treatments. One study found that over a course of 27 injections, intervals between doses averaged  $5.9 \pm 5.4$  months. However, after the 21st treatment, the interval significantly decreased to  $4.6 \pm 1.6$  months ( $p < .01$ ).<sup>10</sup>

**Other drugs.** Other medications, such as anticholinergic drugs, benzodiazepines, levodopa, baclofen, and vesicular monoamine transporter 2 (VMAT2) inhibitors (e.g., tetra-benazine) can also be used, but they are usually not the primary treatment because of their side effect profiles and low efficacy. Eye lubricants can also be helpful to reduce mechanical triggers of BEB.

**Transcranial magnetic stimulation.** In recent decades, repetitive transcranial stimulation (rTCS) has been

explored as a treatment in conjunction with botulinum toxin injections. This adjunctive therapy may be particularly valuable for patients with self-reported anxiety and depression symptoms. In a recent study by Yin et al., the combination of botulinum toxin injections and rTCS showed a significant increase in duration of symptom relief when compared with injections alone (16.89 vs. 13.04 weeks).<sup>6</sup> This could extend the time between injections and reduce the need for pharmacologic adjunctive therapy.

**Surgery.** Surgical options include myectomy of the protractor muscles (corrugator supercili, orbicularis oculi, procerus, and depressor supercili) or facial nerve ablation. Because of their possible complications—which include lymphedema, lagophthalmos, facial droop, disfigurement, or facial anesthesia—these procedures are generally reserved for patients with severe symptoms that do not respond to botulinum therapy.

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