# Oral Methylphenidate for the Treatment of Refractory Facial Dystonias

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***Abstract:*** **Oral methylphenidate (Ritalin, Novartis) has been reported to alleviate symptoms of benign essential blepharospasm in an off-label application. This series presents 3 patients with refractory periorbital and facial dystonias, including blepharospasm, apraxia of eyelid opening, and oromandibular dystonia unresponsive to standard treatments who experienced a response to oral methylphenidate therapy. While the mechanisms for facial dystonias have not been elucidated, there is evidence to suggest that they are on the spectrum with Parkinson disease. Given the role of dopamine loss in the pathogenesis of Parkinson, the authors' speculate that methylphenidate may be acting on the pathway directly involved in facial dystonias. To the authors' knowledge, this is the first report of a case of successful treatment of blepharospasm refractory to upper eyelid myectomy with methylphenidate monotherapy.**

Benign essential blepharospasm (BEB) is a focal cranial dystonia commonly encountered in the oculofacial surgery clinic. Less commonly, patients experience apraxia of eyelid opening (ALO) and associated oromandibular dystonia (OMD), or Meige syndrome. Historically, focal cranial dystonias were thought to be disorders of psychiatric origin. These patients were sometimes treated with psychiatric medicines, including benzodiazepines, antidepressants, and muscle relaxants.[1] These treatments were often unsuccessful, and eventually chemodenervation of the spastic muscles with neuromodulators such as onabotulinum toxin A (Botox; Allergan Inc., Irvine, CA) emerged as the preferred treatment modality. In refractory cases, surgical myectomy of the orbicularis oculi muscle is often used.[1,2] Recently, Price et al.[3] published their findings on the use of oral methylphenidate (Ritalin, Novartis, New York, NY) for the treatment of refractory BEB. Given their success in treating BEB patients with oral stimulant medication, the authors describe the use of oral methylphenidate in refractory facial dystonias. Patient information was deidentified for the purposes of this study, and the study is compliant with Health Insurance Portability and Accountability Act regulations.

## CASE DESCRIPTION

**Case 1.** A 50-year-old woman with BEB and ALO was treated with local injections of Botox for spasms for many years. The patient had persistent spasms and subsequently underwent bilateral upper eyelid myectomy and external levator resection. She had temporary relief after the myectomy, but symptoms recurred. Botox injections were reinitiated, but the patient developed recurrent entropion of the right lower eyelid with injections with resultant corneal irritation. She became intolerant to neuromodulatory therapy and subsequently stopped receiving Botox injections. After a cardiac workup including an electrocardiogram, she was initiated on low-dose oral methylphenidate of 10 mg twice daily. Within weeks, the patient had improvement of the spasms and was able to perform functional tasks such as reading. Within the first 6 months after starting methylphenidate therapy, she resumed driving. She remained free of spasms on oral methylphenidate monotherapy for over 30 months.

**Case 2.** A 37-year-old man with BEB, ALO, and OMD of 13 years' duration had been unsuccessfully treated with oral clonazepam, oral trihexyphenidyl, and finally Botox therapy with moderate success in alleviating his spasms. The patient persisted in having such severe ALO that he used ptosis crutches. He eventually underwent bilateral external levator resection for ptosis as an adjunctive treatment for ALO. However, he remained dependent on the use of ptosis crutches postoperatively. After cardiac clearance, the patient initiated oral methylphenidate therapy. Within weeks of starting therapy, the patient began to experience some relief of spasms. He intermittently uses ptosis crutches and has had improvement in the ALO at more than 1-year follow up. The patient continues to receive Botox injections adjunctively.

**Case 3.** A 58-year-old woman with BEB had been receiving Botox injections for 16 years. Eventually, she developed tachyphylaxis to the medication and began experiencing persistent spasms, despite receiving high-dose, frequent Botox therapy. The patient initiated oral methylphenidate therapy and began experiencing improvement in symptoms within weeks. She remained on oral methylphenidate therapy at 1-year follow up and receives Botox injections adjunctively. Of the 3 patients in this series, none experienced side effects or cardiac complications.

## DISCUSSION

Benign essential blepharospasm and OMD were historically regarded as diseases of psychogenic origin. Modern medicine has recognized this as a neurologic disease, and there is growing evidence suggesting that the disorder may be secondary to dysregulated dopamine levels.[1] Past studies have demonstrated that the neural circuitry involved in BEB is localized to the basal ganglia.[1] More specifically, research in an animal model has shown that depletion of striatal dopamine predisposes rats to developing BEB.[3] These authors suggested that a 2-hit model may lead to BEB: first, a decrease in striatal dopamine, and second, a weakening of the orbicularis oculi muscle leading to enhancement of the trigeminal blink reflex.[4] Depletion of dopamine availability has also been implicated in the pathogenesis of focal dystonias elsewhere in the body.[5]

Another disorder involving dopamine dysfunction is attention-deficit/hyperactivity disorder (ADHD). A substantial body of research has shown that dopamine transporters regulate the level of dopamine available in the synapse.[6] Methylphenidate blocks these dopamine transporters and thereby increases the availability of dopamine in the synapse. Increasing dopamine availability in the brain leads to improved symptoms of attention and motivation in ADHD.[6] The dopamine pathway implicated in this disease maps to a similar location in the brain as the pathways involved in BEB. Therefore, it follows that increasing dopamine availability in the

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synapse of patients with BEB might enhance regulation of the trigeminal blink reflex and thus reduce the misfiring of this pathway that is believed to underlie the symptoms in patients with BEB.

In this small series, the authors report the use of oral methylphenidate as adjunctive therapy in patients with a variety of focal cranial dystonias, including a patient who underwent a complete upper eyelid myectomy and was maintained on methylphenidate alone. All 3 patients were maintained at a dose of 10 mg twice daily. This study limitations include a small sample size and a lack of an objective method to measure response to therapy. It is also possible that the oral methylphenidate had a placebo effect on the patients. Other authors have shown that oral methylphenidate as needed decreases the electromyography response of the orbicularis oculi in patients with BEB.[3] In this series, it was shown that oral methylphenidate can be used as a standing dose and even as monotherapy in patients with refractory dystonias, a finding that has heretofore been unreported and that strengthens the link between dysregulation of the dopamine pathway and the underlying pathogenesis of this disease. Further studies are needed to prospectively examine whether methylphenidate used adjunctively to neuromodulatory therapy improves the treatment of focal cranial dystonias.

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# Punctal Keratinizing Cyst: A Clinicopathological Correlation of an Exceptionally Rare Lacrimal Disorder

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***Abstract:*** **Punctal keratinizing cyst is an extremely rare ectasia arising from the most proximal part of the vertical canaliculus just beneath the punctum. To the best of the authors' knowledge, so far only 1 such case has been described in the literature. Typical clinical features and a meticulous histopathological examination aid in the diagnosis. Although rare, it should be kept in the differential diagnosis of punctal and peripunctal lesions. The authors report the second case with a few clinical and pathologic differences. Addition of more such cases to literature will help unravel the etiopathogenesis of this intriguing punctal disorder.**

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This study has been reviewed by the ethics committee and has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. Informed consent was obtained from the patient.
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Proximal lacrimal outflow disorders involving the punctum include punctal agenesis, stenosis, incomplete punctal canalization, and peripunctal lesions.[1–4] Cystic canalicular lesions are uncommon and do not exhibit keratin deposition.[4–6] Punctal keratinizing cyst is an extremely rare keratin-piling ectasia arising from the most proximal part of the vertical canaliculus just beneath the punctum. To the best of the authors' knowledge, so far only 1 such case has been described in the literature.[7] The authors report the clinical and diagnostic profile and management of a punctal keratinizing cyst along with its clincopathological correlation.

## CASE REPORT

A 52-year-old otherwise healthy woman presented with epiphora in the OS of 1-year duration and a slowly progressive swelling at the medial end of lower eyelid margin of 4 months' duration. This was not associated with any trauma, pain, redness, or discharge. There were no complaints in the OD. Her best-corrected visual acuity was 20/20 in OU and rest of ocular examination was normal.

On examination, the tear meniscus in the OS was found to be elevated. Examination of the medial aspect of the lower eyelid revealed a tense, elevated, dome-shaped cystic lesion in the region of lower punctum, away from the cilia (Fig. 1A). The wall appeared transparent all around except in the central area, which showed a creamy white discoloration (Fig. 1B). Examination at high magnification showed focal areas of vascularization on the slopes of the dome (Fig. 1B). However, the punctum could not be visualized (Fig. 1A,B). The architecture of the pars lacrimalis and the pars ciliaris portion of the eyelid was normal. The left upper punctum and the lacrimal system of the fellow eye were normal.

The patient underwent an excision biopsy, and care was taken not to extend the incision beyond the surface of the eyelid margin to avoid trauma to the vertical canaliculus (Fig. 1C). A white creamy material was found pouting out and following its clearance, the punctum, although with a narrow orifice, was found to be intact with the inner walls of the vertical canaliculus showing mucosal folds and mild mucosal edema (Fig. 1D). Probing revealed the lower horizontal canaliculus to be normal, and the lacrimal system was patent on irrigation through the punctum. The patient was advised tapering doses of topical steroid-antibiotic drops. At 6-week follow up, the punctum was well seen with a good opening with grade 1 dye disappearance and the patient reported resolution of epiphora.

**Histopathology.** Gross examination revealed a thin grayish white soft tissue measuring 3 × 2 mm without any areas of hemorrhages. Microscopic examination showed a crenellated cyst wall lined by a multilaminar keratinizing stratified squamous epithelium (Fig. 2A). The epithelium was multilayered and showed a regular basaloid germinal layer without any goblet cells or any granular layer (Fig. 2B). The