Case Report

Treatment of Benign Essential Blepharospasm and Idiopathic Hemifacial Spasm with Vimpat® (Lacosamide)

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Abstract

Background

Benign essential blepharospasm and hemifacial spasm are currently treated with botulinum toxin therapy, eyelid protractor myectomies, and microvascular decompression of the facial nerve or pharmacologic therapies including anticonvulsants. Because of limited treatment success in some patients, another treatment option is needed.

Methods

Lacosamide (Vimpat®), a novel anticonvulsant released in 2008 for the treatment of partial-onset seizures, was used to treat nine patients. Four patients had hemifacial spasm and four were diagnosed with benign essential blepharospasm. A ninth patient had both benign essential blepharospasm and hemifacial spasm. Lacosamide selectively enhances the slow inactivation of voltage-gated sodium channels resulting in stabilization of hyperexcitable neuronal membranes and inhibition of repetitive neuronal firing.

Results

Lacosamide provided rapid and significant relief of hemifacial spasm and benign essential blepharospasm at doses ranging from 50 mg bid to 200 mg bid. The symptomatic relief has been sustained in all patients over a period of years.

Conclusions

Lacosamide provided effective symptomatic relief in nine patients with either hemifacial spasm or benign essential blepharospasm. Our experience suggests that lacosamide is a potentially valuable adjunct in the management of these conditions. Nevertheless, the long-term efficacy of lacosamide in hemifacial spasm has yet to be determined.

Keywords: Hemifacial Spasm; Benign Essential Blepharospasm; Vimpat; Lacosamide; Anticonvulsant

**Introduction**

Benign essential blepharospasm (BEB) is a syndrome characterized by excessive or continuous bilateral eyelid closure due to spasm of the orbicularis oculi and adjacent muscles. BEB is considered to be a form of focal dystonia caused by basal ganglia dysfunction. Additionally, brain imaging and electrophysiologic studies suggest pathologic changes in excitability in the anterior cingulate, primary and secondary motor areas [1]. BEB is typically a chronic disorder, but up to about 10% of patients may have a spontaneous remission. Most remissions occur within the first 5 years [2]. BEB is often associated with other oromandibular dystonias.

Hemifacial spasm is characterized by a combination of unilateral clonic and tonic spasms of the muscles innervated by the facial nerve. The most common cause of hemifacial spasm (HFS) is now widely recognized as neurovascular contact or compression at the root exit zone of the facial nerve at the lateral pons [3,4]. The movement disorder typically begins in the orbicularis oculi and over the course of years involves the brow, mid and lower face, and neck platysma. The prevalence rate of hemifacial spasm is estimated to be 14.5 per 100,000 in women and 7.4 per 100,000 in men [5,6]. The age of onset is typically between 40 to 50 years of age. Hemifacial spasm, if untreated, is a lifelong condition, and less than 10% of patients experience spontaneous remissions [6]. The medical therapy of choice for HFS is botulinum toxin (BTX).

**Methods**

Patients included in this case series were encountered over a period of six years as they presented to the first author’s neurology and sleep disorders practice. The patients were treated with lacosamide following their initial evaluations and after counseling as to the expected results and potential side effects of the medication.

**Cases**

**Patient 1**

A 52 year old female occupational therapist presented with a complaint of continuous involuntary twitching of the entire left side of her face. The facial twitching began following a cervical laminectomy procedure in 1999. Initially, only the orbicularis oculi muscle was involved, but the mid and lower face was involved within a month. Treatments with BTX were started in 2000; and these provided temporary partial relief.

Physical examination showed frequent, recurrent spasms of the left side of the face. Contrast MRI of the brain showed a normal brainstem and craniocervical junction. Computerized Tomography Angiography (CTA) imaging of the cerebral vessels revealed redundancy of the vertebral arteries. Brainstem evoked potential testing showed findings consistent with an ipsilateral lower brainstem lesion between the acoustic nerve and lower pons.

The patient was started on lacosamide on a trial basis for her hemifacial spasm during a hospitalization event. At a dose of 150 mg twice per day she reported 60 to 70% improvement in her spasms. The lacosamide was discontinued at hospital discharge and her hemifacial spasm returned. At her office follow-up visit, the previous dosage was re instituted with similar results within 24 hours. And, when stress free, she described 80% relief with side effects. With stress, however, HFS control deteriorated to 40%. When the lacosamide dose was increased to 200 mg by mouth twice a day, she reported 90% improvement with deterioration to 70% when under stress. This dose was tolerated well and after one week was increased to 250 mg twice a day. At this dose, the patient reported 99% improvement and was able to sing in the choir again, suck from a straw and whistle without worsening of the spasms. However, at this dose she reported the onset of a hand tremor. The hand tremor interfered with signing her name and texting on her telephone. She also complained that her balance was affected at that dose. When the dose of lacosamide was reduced to 200 mg during the day and 250 mg at bedtime, she experienced significant improvement of the hand tremor and had no hemifacial spasms present the next day. Follow up has continued since beginning therapy six years ago. The patient continues to have greater than 90% hemifacial spasm relief.

**Patient 2**

A 53-year-old female employed as a certified nursing assistant was initially evaluated after being hospitalized for a seizure. Left hemifacial and bilateral blepharospasm were noted during that evaluation. The patient reported that her conditions began in 1999 following a motor vehicle accident and subsequent cervical spine surgery. The symptoms initially involved both eyes. However, the left HFS developed within months. She began BTX treatment in 2002. In addition to BTX therapy she underwent bilateral protractor myectomies. On months when BTX therapy was omitted, she described episodic head shaking that occurred throughout the day and “fender-benders” due to hypersensitivity of her eyes to sunlight. Monthly BTX therapy provided up to 50% symptom relief; but over the previous three years that therapy had become less effective.

Initial physical examination showed near continuous twitching of the left face and blepharospasm of her eyes. A contrast and non-contrast MRI of the brain showed no abnormalities of the brain or brainstem. The electroencephalogram showed epileptiform discharges in the left posterior temporal and parietal region. Auditory brainstem evoked potentials were normal.

Lacosamide was started as a treatment of her seizure disorder and as an intentional therapeutic trial for the HFS. When taking 100 mg by mouth twice per day, she had no significant change in her BEB and hemifacial spasm, but when the lacosamide...
dose was increased to 100 mg three times per day, she reported a 60% reduction in blepharospasm and 95% relief of her hemifacial spasm. When the dose was increased to 200 mg twice per day, she had complete blocking of the hemifacial spasm with an estimated 95% blepharospasm inhibition. Due to the extent of her symptom relief since beginning lacosamide she has not returned for BTX therapy. Furthermore, the patient is able to work at a computer and read without holding a book inches from her face. The patient has continued to have BEB and HFS control since beginning lacosamide therapy in 2010.

**Patient 3**

A 65-year-old female patient reported onset of symptoms 16 years ago but she was not diagnosed with BEB until 2011. The spasms reportedly started in the right eye and as it worsened, involved the left eye as well. The blinking was described as uncontrollable and made worse by talking, bright lights and was especially worse when driving. When her spasms worsened, she would use alprazolam (Xanax®). This medication seemed to reduce the severity of the spasms but did not make them stop. When she presented to the clinic, she was receiving BTX injections every two months. After discussion of treatment options, the patient decided to begin a trial of lacosamide in March of 2013. At a dose of lacosamide 100 mg BID, she had no twitching and eye blinking “felt normal”. She found that she was able to drive and enjoy the scenery because now her eyes could focus and tolerate light. She found that this dose gave her 100% BEB relief but only as long as she continued BTX injections every 3 months. She did not like BTX injections because each treatment resulted in two to three weeks of blurred vision and puffy eyelids. Lacosamide caused some memory complaints and a tolerable intermittent hand tremor. She stated that without lacosamide she could not drive or be employed. She currently continues to take the 100 mg bid of lacosamide along with scheduled maintenance BTX treatments. She stated that if she misses a BTX treatment, she is still able to drive.

**Patient 4**

In February 2012 a 74 year old female patient with BEB presented requesting lacosamide therapy after hearing about it from a friend. She stated that she had always had light sensitivity and constant eye blinking and her husband stated that this problem was present as far back as high school. She stated that in high school, her eyes felt as if they were being forced closed and it required her conscious effort to keep them open. She typically would wear dark glasses during the day and she could see better at night. She had found that postauricular 1.5 mg Scopolamine patch was very helpful but she experienced unpleasant withdrawal symptoms when taken off the medication. Her usual BTX injections were bi-monthly but BTX would give only 50% relief for approximately one month. Following the introduction of lacosamide she reported an 80% improvement in her eye symptoms, but also experienced an unpleasant “smothering” sensation. She has been able to tolerate lacosamide 50 mg BID with 80% relief but finds that she needs to continue BTX injections every 3 months in order to maintain that degree of improvement.

**Patient 5**

When first seen in 2012, this 59 year old female patient stated that she had mild BEB for at least 5 years prior to worsening of the condition following a 2007 motor vehicle accident. She was diagnosed with BEB in 2009. In addition, she reported occasional “vocal cord spasms” that occasionally made it difficult to speak. At some point she began having chemodenervation with BTX every two months. She underwent surgical procedures consisting initially of a basic eyelid and eyebrow lift in November 2010 followed by bilateral levator myectomy. Prior to this second surgery, she could see only by holding her eyes open from the forehead. She was so incapacitated that her parents had to be her chauffeurs. When she started lacosamide, she was gradually titrated to 200 mg bid with 50 to 60% improvement. She was able to decrease her BTX dose from 55 units to 33 units of Botox and changed from bi-monthly BTX to treatment every 3 months. She was followed for two years but has subsequently been lost to follow up.

**Patient 6**

In 2012, this 65 year old female patient presented with a four month history of BEB. In addition to the BEB, she reported having bilateral spasms in the lower part of her face. She reported difficulty keeping her eyes open when she was fatigued. She had tried clonazepam but it made her too drowsy. Prior to being seen for her initial clinic visit, she reported having had a total of two BTX treatments. Her brain MRI was reported as normal. When she started treatment with lacosamide and after it had been titrated to 150 mg bid, she complained of vision blurring as if her lens prescription was “too strong”. Since then she has remained stable on a dose of lacosamide 100 mg bid and reports approximately 85% relief. BTX treatment by itself had reportedly provided her only 45 percent relief. She continues to have botulinum injections every two months. With lacosamide, she is able to drive but describes having some difficulty driving approximately two weeks prior to the next BTX treatment.

**Patient 7**

A 74 year old female patient presented with a four year history of right HFS involving the eye and face. Her work up included an MRI of the brain that showed mild cortical atrophy and mild small vessel disease. She was previously treated with several courses of BTX injection therapy without relief. Since she had failed other treatments, we decided to begin her on lacosamide 100 mg orally bid. The patient reported that she had relief but the hemifacial spasm reoccurred when she awakened in the mornings. After the dose of lacosamide was increased to

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200 mg bid, she reported an estimated 80% hemifacial spasm improvement. She continues lacosamide without adverse side effects.

**Patient 8**

A 68 year old female patient first presented for evaluation in June 2015 and was diagnosed with left sided HFS. Her family doctor had been treating her for “trigeminal neuralgia” with 1200 mg of gabapentin in divided doses and then later with 600 mg oxcarbazepine. Her examination was clearly that of left sided HFS and while titrating her off of gabapentin and oxcarbazepine, we initiated lacosamide 50 mg 1 or 2 tablets orally bid. When she returned in August 2015, she reported 50 to 60% HFS improvement but she still had increased facial spasms when emotionally upset. She was instructed to take lacosamide 100 mg bid. When she returned one month later, she reported that she was still having twitching of the left eye and cheek and asked to increase her dose. She was then prescribed lacosamide 150 mg bid. When she returned two months later, she reported that lacosamide had completely stopped her facial spasm and without any side effects. When the patient was seen in follow up in January 2016, she continued to have completely controlled the HFS.

**Patient 9**

A 77 female year old patient afflicted by left HFS since 34 years of age presented for evaluation. She had tried biannual BTX injections and was happy with the benefit that they provided but found that their therapeutic improvements were short lived requiring repeated treatments. An MRI was performed and reported as normal before she was started on lacosamide 150 mg bid in January 2015. In March 2015, she stated that lacosamide had provided 85% HFS relief. However, she reported that her HFS spasms worsened whenever she worked at the computer, while reading or when experiencing stress. Due to the cost of lacosamide, she reduced her medication dose to 150 mg once per day. On the once per day lacosamide regimen she continued to report 70% HFS improvement. When seen in October 2015, the patient had received lacosamide patient assistance and had returned to 150 mg bid dosing with 75% improvement. She also reported opting to no longer receive BTX. She is currently experiencing 85% HFS relief taking lacosamide 200 mg bid.

**Discussion**

Botulinum neurotoxin (BTX) is the medical therapy of choice in benign essential blepharospasm and hemifacial spasm [7,8]. However, the therapeutic effect is sometimes insufficient and repeated BTX injections are often required. Unfortunately, repeated BTX injections have associated limitations. These include high costs and the potential for denervation of the injected muscles. Other treatment options include various oral pharmacologic therapies that have shown limited efficacy [9].

Lacosamide (Vimpat®) was initiated because of the success of other antiepileptic drugs (AEDs) in the treatment of HFS [11-16]. Anticonvulsants have been useful for hemifacial spasm most likely due to their ability to inhibit repetitive neuronal firing. However, anticonvulsant therapy is often limited by side effects or a limited response to therapy. Lacosamide is a novel AED licensed as adjunctive therapy for partial-onset seizures with or without secondary generalization [17]. Lacosamide is an agent with a low toxicity profile and has a novel mode of action. It appears to be different from existing AEDs in that it selectively enhances the slow inactivation of voltage-gated sodium channels resulting in stabilization of hyperexcitable neuronal membranes and inhibition of repetitive neuronal firing [18-20]. Lacosamide is generally well tolerated and the most common adverse events are nonspecific central nervous system effects such as dizziness, vertigo, headache and nausea [21,22].

**Conclusion**

In this case series, we reported 9 patients with benign essential blepharospasm or hemifacial spasm who were treated successfully with lacosamide. Ours is the first case series reporting successful treatment of these conditions with lacosamide. Since lacosamide is not approved by the Food and Drug Administration (FDA) for this condition, treatment of both HFS and BEB is an off-label use of the medication. The medication has an acceptable toxicity to therapeutic ratio and serum levels are not required. The lacosamide package insert recommends that patients with renal impairment and those with severe cardiac disease and conduction defects should be monitored. Neutropenia, agranulocytosis and worsening of depression have been reported. The medication may be expensive for patients without prescription coverage but patient assistance programs are available for most patients. Finally, the long-term efficacy of lacosamide in benign essential blepharospasm and hemifacial spasm has yet to be determined.

**Author Contributions**

Dr. Gary Mellick provided the case patients, collected reference articles and composed the initial draft of the article. He serves as the corresponding author for this manuscript and its revision.

Dr. Larry Mellick collected reference articles and contributed equally to the writing of the article.

**Financial Disclosure Form**

Dr. Gary Mellick serves as legal consultant for work related injuries and is retained by Actavis, Lupin, Teva and Sandoz in a joint consulting agreement.

Dr. Larry Mellick contributes to a monthly blog for Emergency Medicine News and occasionally serves as a consultant in medical malpractice cases.

References


