whole sample of patients; subjects who dropped out were considered with the last observation carried out.

No statistical significance was found by applying the ANOVA for repeated measures to compare clinical features in the two groups during the 8 months, although statistical significance was approached when comparing the MMSE scores ($P = 0.06$) (Fig. 1). After 6 months of treatment, patients on rivastigmine showed a significant increase in MMSE score compared with the basal condition.

The AIMS was almost the same in the two groups. The control group exhibited a significant increase in hyperkinesia scored by M&Q and AIMS scales (Fig. 1). Mean TFC scores at baseline were 6.53 and 8.57 for the active and control group, respectively (lower scores indicate worse functional capacity), and after 8 months of treatment were reduced significantly in both groups (Fig. 1).

Discussion

The results of this study suggest a trend for improved cognitive performance on MMSE in the active treatment group compared with that in the control group. This may suggest that rivastigmine improves cognitive function in HD patients, given that this was a small study. Moreover, comparison of cognitive evolution between treated and nontreated patients approached statistical significance. A larger study should be carried out to evaluate if these results can be confirmed.

Rivastigmine did not seem to reduce hyperkinesia, but during the study period it did seem to slow the worsening of chorea in the rivastigmine group compared with that the control group. The control group showed a clear increase in involuntary movements during the 8 months, although this effect was not strong enough to produce a difference in the development of neurological impairment between the two groups. The global severity of HD, as expressed by TFC score, seemed to worsen in both groups, although the deterioration of functional capacity was less pronounced in those patients on rivastigmine.

The improvement of cholinergic transmission in HD may slightly reduce the development of the disease, and this effect is mediated probably by striatal interneuronal and cortical neuronal activation. Considering that rivastigmine was well tolerated in the patients of this study, the efficacy of this drug in slowing the progression of the disease might be tested in long-term clinical trials.

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Substantial Improvement in a Meige's Syndrome Patient With Levetiracetam Treatment

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Abstract: We report on a woman with idiopathic Meige's syndrome whose dystonia improved with the use of levetiracetam (LEV, Keppra, UCB Pharma, Smyrna, GA). This report

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and data from an animal model of paroxysmal dystonia suggest that LEV might be helpful in the treatment of dystonia. © 2004 Movement Disorder Society

Key words: Meige's syndrome; cervical dystonia; levetiracetam; Keppra

Meige's syndrome, a form of focal dystonia, is characterized by blepharospasm and involuntary movements of the lower face, jaw, and neck.[1] The condition can be disabling. Blepharospasm can impair a patient's ability to read, drive a motor vehicle, or write, and in its severest form, can cause functional blindness.[2] Dystonia of the lower face can result in difficulty with speech, eating, and swallowing.[3–6]

The pharmacologic treatment of Meige's syndrome is challenging, and currently available medications have demonstrated limited efficacy. Medications that have been reported to be of some benefit include those with dopaminergic, antidopaminergic, or anticholinergic properties as well as agents used to treat spasticity.[7–14] Botulinum toxin injections have a beneficial but transient effect on eyelid and oromandibular dystonia,[15–17] but weakness is a common side effect limiting their use.

Recently, in a hamster model of paroxysmal dystonia (a form of idiopathic generalized dystonia), levetiracetam (LEV, Keppra, UCB Pharma, Smyrna, GA) was reported to significantly reduce the severity of dystonia.[18] This preclinical observation raised the possibility that patients with dystonia might be treated with LEV. We present a patient with Meige's syndrome who was treated with LEV and who experienced a substantial improvement in blepharospasm and oromandibular dystonia.

Case Report

The patient is a 56-year-old woman who developed bilateral blepharospasm and oromandibular dystonia in 1994 and was diagnosed with Meige's syndrome. Due to dystonia, she had difficulty chewing and eating and was unable to perform a variety of daily activities, including driving, reading, writing, and watching television. Her past medical history was unremarkable, and she had no history of head trauma or exposure to neuroleptic medications.

The patient was evaluated and treated by several general neurologists and ophthalmologists over the ensuing 9 years. Blood work taken during that time, including serum chemistries and ceruloplasmin was normal, as were magnetic resonance imaging scans of the brain and cervical, thoracic, and lumbar spine performed with and without contrast. Ophthalmologic examinations excluded abnormal ocular conditions such as corneal abrasions, congenital glaucoma, and Kayser-Fleischer rings. She was treated with tranquilizers and anticonvulsant medications, including clorazepate (7.5 mg b.i.d.) and gabapentin (400 mg t.i.d. for 2 months), with little or no resolution of symptoms by self-report. Botulinum toxin A injections were performed in 1997, and a total of 100 units was injected into the orbicularis oculi, corrugator, orbicularis oris, and masseter muscles bilaterally. The injections resulted in improvement in symptoms for 6 months and were repeated once with only mild and temporary improvement of symptoms. A bilateral orbicularis oculi myectomy was performed in 1998 that did not provide symptomatic benefit.

The patient was evaluated at a university movement disorders center in Tampa in 2003 by a movement disorders specialist (T.A.Z.). Neurological examination revealed bilateral blepharospasm and involuntary dystonic spasms of the lower facial muscles consistent with a diagnosis of Meige's syndrome. She also suffered from mild cervical dystonia of which she was unaware.

The patient was started on LEV 500 mg/day for 5 days and was titrated to 500 mg t.i.d. within the next 10 days. She indicated that the blepharospasm and oromandibular dystonia improved greatly with LEV 500 mg/day, and resolved with 500 mg t.i.d. She has remained on LEV for 19 weeks, with sustained and excellent improvement in dystonia. The patient reports that her dystonic symptoms worsen if she does not take LEV on time (within 8 hours) or if she forgets to take a dose.

To quantify improvement, two physicians blind to her condition independently rated videotapes of the patient using the Fahn–Marsden (F-M) scale.[19] The F-M scale evaluates dystonia in nine body areas, including eyes, speech and swallowing, mouth, neck, trunk, right arm and leg, and left arm and leg. In each body area, there is a severity rating (range = 0–4 [maximum]) and a provoking factor rating (range = 0–4 [maximal dystonia that is present at rest and does not require provocation]). The maximum subscore for the eyes (0–8), mouth (0–8), and neck (0–8) dystonia is 24. The first rater (E.D.L.) was unfamiliar with the patient's history and treatment, whereas the second rater (a movement disorder specialist, R.A.H.) was blinded to the order of pre- and posttreatment assessments. The F-M scores of the first rater were 10 (eyes 8, mouth 1, neck 1) before treatment with LEV, and 4 (eyes 4, mouth 0, neck 0) after treatment, whereas the scores of the second rater were 12 (eyes 8, mouth 1, neck 3) and 4 (eyes 4, mouth 0, neck 0) pre- and posttreatment, respectively. The patient can now read, drive, and watch television as a result of a reduction in blepharospasm. The oromandibular dystonia has also improved, alleviating her difficulty while chewing and eating (see video Segment 1).

Discussion

Meige's syndrome is a potentially disabling form of focal dystonia. The neurochemistry of the disorder remains unknown.[20] Dopamine agonists and a variety of other medications have demonstrated limited efficacy in treating the condition.[15,20,21] Peripheral neurectomy of the facial nerve has been performed to treat blepharospasm, but the procedure is associated with high recurrence and complication rates.[22–24] Myectomy has been demonstrated to improve blepharospasm,[25–29] but complications include forehead numbness and cosmetic deformities of the eyelid.[24,27,29] Botulinum toxin injections generally have a beneficial but transient effect.[15] Deep brain stimulation (DBS) has been used recently to treat dystonia, and pallidal DBS was reported to improve blepharospasm and oromandibular dystonia in 1 patient with isolated Meige's syndrome over a 2-year period.[30] Botulinum toxin injections and limited myectomy were unsuccessful in treating dystonic symptoms in our patient.

Spontaneous remission of symptoms in our patient is possible but improbable. Remission of essential blepharospasm and Meige's syndrome has been reported, but is uncommon.[31–33] One retrospective study found that 11.3%

of patients with either essential blepharospasm or Meige's syndrome experienced a spontaneous resolution of symptoms after a mean of 4.9 years from symptom onset (range, 3 months to 22 years).[31] Approximately 75% of patients who demonstrated a complete remission of symptoms did so within 5 years of disease onset. Another study found that only 2.5% of patients had remission of symptoms.[33] Although we cannot fully exclude spontaneous remission as the cause of symptom resolution in our patient, several factors argue against this possibility: (1) the rarity of spontaneous remission, (2) the temporal link between onset of therapy and resolution of symptoms and signs, and (3) the observation that the patient experiences a recurrence of dystonic symptoms after withholding a dose of LEV or when she does not take LEV on time.

LEV is an antiepileptic medication that is approved as monotherapy or as an adjunct to treat partial-onset seizures.[34,35] It is a structural analogue of piracetam, a drug that effectively reduces cortical myoclonus but is not approved for use in the United States.[36] The exact mechanisms of action of LEV as an antiepileptic agent are unknown.[18] Case reports and small open-label trials indicate that LEV reduces cortical reflex myoclonus due to various causes and is generally well tolerated.[37] Another case report found that piracetam reduced choreoathetosis.[38]

Loscher and Richter studied the effects of LEV and piracetam in a mutant hamster model of paroxysmal dystonia, a form of idiopathic generalized dystonia, and found that both drugs significantly decreased the severity of dystonia.[18] The latency to onset of dystonic attacks was increased and the severity of dystonic attacks was decreased in these animals. This finding suggests that LEV may have antidystonic properties. This preliminary evidence and our case report indicate that LEV might be helpful in the treatment of dystonia. Controlled clinical trials are warranted to assess its safety and efficacy.

Legends to the Video

The patient is a 56-year-old woman who has Meige's syndrome and cervical dystonia.

Segment 1. The patient before treatment shows moderate blepharospasm, mild oromandibular dystonia, and mild cervical dystonia.

Segment 2. The patient on levetiracetam 500 mg t.i.d. demonstrates substantial improvement in blepharospasm, oromandibular, and cervical dystonia.

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