Clinical Note

Hemifacial Spasm: Successful Treatment with Felbamate

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Abstract

Medical treatment of hemifacial spasm has generally been ineffective. This report describes a 36-year-old man with a 7-year history of right hemifacial spasm who responded to felbamate (Felbatol®) at doses of 1800-2800 mg per day. During treatment, he was able to achieve complete control of all spontaneous facial muscle spasms at rest. Activated hemifacial spasms, initiated by chewing, speaking, smiling, or grimacing were reduced in frequency and intensity of contraction by 40%-50%. Spontaneous worsening of the hemifacial spasms occurred at a dose of 3600 mg/day. Control of the hemifacial spasm was regained at a lower dose. This is the first reported use of felbamate for the control of hemifacial spasm. Microvascular decompression of the facial nerve has been the only known effective treatment for this condition. Successful felbamate therapy would provide an alternative to those patients for whom surgery is not a treatment option.


Key Words
Felbamate, Felbatol®, hemifacial spasm, facial nerve, anticonvulsant therapy

Introduction

Hemifacial spasm, a rare condition without a known true incidence, appears to be the motor analogue of trigeminal neuralgia. While trigeminal neuralgia is a paroxysmally painful sensory condition of the trigeminal nerve and ganglion, hemifacial spasm affects the facial nerve and manifests as pure motor hyperactivity. Except for a report of successful treatment of hemifacial spasm using baclofen (37.5 mg/day),¹ microvascular decompression of the facial nerve has been the only known effective treatment for this condition.

Felbamate (Felbatol®) is a new anticonvulsant used as monotherapy or adjunctive therapy in adults who have generalized tonic-clonic seizures or refractory partial onset seizures and in children with generalized seizures of Lennox-Gastaut.²⁻⁵ This report describes effective treatment of a patient with hemifacial spasm using this drug.

Case Report

This 36-year-old sales account manager first noted onset of right hemifacial spasm in March 1987. For the first 5 months, the hemifacial spasm was intermittent and associated with a deep lancinating pain in the right neck and shoulder, which resolved spontaneously. Subsequently, he developed severe right-sided headaches thought to be due to the frequent facial muscle spasms. In August 1987, a neu-
rologist prescribed carbamazepine 600 mg per day and aprazolam 2.0 mg per day, which were discontinued 2 months later when the patient saw no improvement in his condition. Two years after the onset of the hemifacial spasm, he underwent evaluation with computerized tomography, auditory brainstem evoked potentials, and visual evoked responses, all of which were normal. Magnetic resonance imaging showed numerous areas of hyperintensity in the deep white matter of both cerebral hemispheres in a pattern characteristic of demyelinating disease. When he presented in September 1993, he was noted to have frequent intermittent uncontrolled brief repetitive spasms of the right facial musculature, most prominent in the midface. His face would draw up and his right eye briefly close with most spasms. He reported that his condition typically worsened with fatigue, lack of sleep, fear, and anxiety. It usually improved with physical activities, such as running or walking. His previous medical history was significant only for right abdominal wall herpes zoster 1 year prior to the onset of the hemifacial spasm. General medical examination was normal. The neurologic examination showed only slight right facial paresis. He had normal hearing when evaluated by finger rubbing, Rinne, and Weber tests.

After appropriate discussion of the current treatment options available to the patient and customary use of this medication, a trial of medical therapy with felbamate was initiated. While taking felbamate at a dose of 2400 mg/day, the patient noted complete cessation of all spontaneous facial muscle spasm. He continued to have intermittent hemifacial spasm when he voluntarily activated his facial musculature, but this was 40%-50% reduced in frequency and intensity of contraction than before therapy. When medication was discontinued inadvertently, the patient experienced a return of the hemifacial spasm. Higher doses of felbamate, up to 3600 mg/day, resulted in a loss of therapeutic effect and spasms that seemed to be more severe than those prior to taking any medication. Upon returning to a lower dose of felbamate (2800 mg/day), the patient successfully regained control of an estimated 80% of his spontaneous facial activity and 20%-40% of the spasms associated with facial muscle activation. Except for moderate xerostomia and mild dyspepsia, felbamate was well tolerated even at higher doses. The patient remarked that, while on felbamate, he felt his quality of life had improved significantly, he was sleeping better, and he felt more energetic.

**Discussion**

The mechanism by which felbamate is able to control hemifacial spasm is presently unknown. Rho and colleagues have shown that felbamate acts at both the N-methyl-D-aspartate (NMDA) and gamma-aminobutyric acid (GABA) receptors in cultured rat embryo hippocampal neurons. McCabe and collaborators have determined that felbamate can interact with the glycine site on NMDA receptors, but this action does not appear to account for its antagonism of NMDA responses in hippocampal neurons. Potentiation of GABA-mediated inhibition is a well-recognized anticonvulsant mechanism shared by several marketed and investigational antiepileptic drugs. In a like manner, drugs that blockade NMDA-type excitatory amino acid receptor responses are known to have anticonvulsant properties and, as with felbamate, neuroprotective activity. Felbamate is the first anticonvulsant drug with twofold actions on excitatory (NMDA) and inhibitory (GABA) brain mechanisms. GABA-potentiating drugs typically cause sedation and other central nervous system (CNS) depressant side effects. In contrast, NMDA antagonists are not depressants, but typically produce behavioral activating effects at low doses and dissociative anesthesia at high doses. In seizure protection the effects on GABA and NMDA receptors are likely to be synergistic. In controlling the hemifacial spasm the actions may be synergistic or may be primarily due to inhibition of the NMDA recognition sites. The location of felbamate action is likely to be at the site of lower motor neuron pathology.

Recently, aplastic anemia and hepatic failure has been identified in patients receiving felbamate for anticonvulsant therapy. In August 1994, the manufacturer of this drug issued a letter of warning to all practitioners, at the suggestion of the US Food and Drug Administration (FDA), recommending that patients be withdrawn from felbamate (Felbatol), unless,
in the physician’s judgment, the patient’s well-being is so dependent upon continued treatment with felbamate that withdrawal is deemed to pose an even greater risk.

There is still insufficient information available to provide a precise estimate of the incidence of felbamate-associated aplastic anemia and hepatic failure as a substantial fraction of patients beginning treatment with felbamate did not remain on it throughout the entire period of potential risk (which, based on the cases reported, spans an interval from at least 5 to 30 weeks). The crude incidence of aplastic anemia due to the drug, which has been reported to be 20/100,000 or 1/5,000 based on 21 reports arising from a population of approximately 100,000 patients (estimate made based on prescriptions written), is almost certainly a substantial underestimate of the true risk. Accordingly, the risk may be closer to 1 in 2,000 or greater among patients remaining on the drug for longer than a few weeks. The time of onset of the aplastic anemia from the time of treatment initiation with felbamate has ranged from approximately 5 to 30 weeks, and the mean time to onset among cases for whom the information is available (N = 18) is 128 days. It is clear that the risk is not transient. How long the risk persists and whether its magnitude changes with time are not known.

Eight cases of acute liver failure, including 4 deaths, have also been recently reported in association with the use of felbamate. Although full information is not yet available, the number of cases reported greatly exceeds the number that is expected based on the annual incidence of acute liver failure in the United States (that is, about 2,000 per year). The cases included patients of both genders, ranging from 5 to 78 years in age. Seven of the eight patients were taking concomitant drugs, including other anticonvulsants and nonprescription drugs. In several of the cases, there were nonspecific premonitory signs, but in others, the patients were already in frank liver failure at the time their illness was detected. The time between initiation of treatment with felbamate and diagnosis of the cases ranged from 14 to 257 days. Although the fragmentary nature of the information available precludes a definitive conclusion about the exact role played by felbamate, there is no question that patients on felbamate must be monitored closely for signs of liver injury. At a minimum, patients should be evaluated prior to treatment initiation for evidence of preexisting liver damage. Whether preexisting liver disease increases the risk of fulminant hepatic failure is unknown, but it seems prudent to avoid the use of felbamate in any patient with preexisting liver pathology. Once felbamate is initiated, ALT, AST, and bilirubin should be monitored on a weekly basis. Whether early withdrawal from treatment following the first sign of liver injury can reduce the risk of subsequent fulminant liver failure cannot be known with certainty; nonetheless, patients developing laboratory findings indicating liver injury should be immediately withdrawn from treatment.

Because of its association with these toxicities, the use of felbamate is presently indicated for use only in those patients who respond inadequately to alternative treatments and whose epilepsy is so severe that a substantial risk of aplastic anemia is deemed acceptable in light of the benefits conferred by its use. The information on potentially fatal liver injury gives further reason to limit the use of felbamate to the most severe and refractory patients.

Before prescribing felbamate, physicians should be thoroughly familiar with the details of the revised prescribing information provided by Wallace Laboratories.13 Recently, the FDA Peripheral and Central Nervous System Drugs Advisory Committee has recommended that felbamate’s marketing be continued with appropriate labeling revisions. In addition to new warnings regarding aplastic anemia and hepatic failure, a “Patient Information/Consent” section has been added to the revised package insert which should be thoroughly reviewed with any patient currently taking felbamate or any new patient for whom the doctor intends to prescribe the anticonvulsant.14

**Conclusion**

Felbamate appeared to be an effective medical treatment for hemifacial spasm in this patient. However, due to the recently identified incidences of aplastic anemia and hepatic failure associated with its use, patients should be carefully selected according to need for therapy and the risk–benefit ratio. All patients should be adequately warned in writing and a signed informed consent to therapy should be carried out prior to initiating felbamate.
therapy. If treatment effectiveness is verified in other patients, felbamate use may be indicated for some hemifacial spasm patients who are unable to tolerate surgery. The medical therapy for hemifacial spasm will need further clinical trials to establish its true effectiveness and more research to understand better its physiological mechanisms, sites of action, and long-term effects.

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References


