Update: Treatment of Essential Tremor

Case Presentation

A 68-year-old man with a 9-year history of essential tremor (ET) presented to the university movement disorders clinic with the primary complaint of upper-extremity tremor. He noted that certain daily activities have become more difficult to perform, including dressing, attending to personal hygiene, writing, drinking, and feeding. The patient worked as a professional carpenter until symptoms precluded continuation. He is now retired. The patient recalled a family history of ET affecting his brother and uncle, and reported only a modest reduction in tremor after self-administration of ethanol. His past medical history consists of type II diabetes. No signs of other neurologic diseases were present. An MRI of the patient's brain with T3 images performed within the past 6 months was normal. The patient's medication list at the time of this clinic visit included propranolol long-acting (LA) 80 mg QD (for tremor) and glipizide-metformin 5 mg/500 mg TID. Intensification of propranolol treatment was dose-limited by side effects of hypotension, bradycardia, and reflex tachycardia, which resolved when the propranolol dose was lowered.

A 10-topic review of systems was performed and was negative except for a recent weight gain of 5 lbs and constipation. On examination, the patient appeared healthy except for the tremor of his hands. Pulse was 58, BP 126/78, and RR 12. He had no bruits over the neck. Mini-Mental State Examination result was 30 out of 30. He had normal visual fields, visual acuity, eye movements, pupillary responses, facial sensation and movement, hearing to a 512-hz tuning fork, palate movement, tongue bulk and movement, neck flexion and extension, and SCM strength. Muscle tone, bulk, and power were normal in both arms and legs. Routine gait was normal, and he was able to tandem walk and heel walk. There was a mild decrease in pinprick in a stock-glove distribution bilaterally in his upper and lower extremities, a mild decrease in vibratory sense in his lower extremities, normal position sense in all extremities, and 1+ reflexes in his extremities. Coordination was normal on finger-to-nose except for a tremor. He possessed a moderate bilateral action tremor, with his dominant (right) hand being the most affected.

The head MRI scans were personally reviewed, and the examiner agreed the studies were normal. Also normal were outside labs of a CBC, CMP, and urinalysis.

The patient was started on primidone 25 mg BID for the first 5 days of treatment, and the dose was titrated upward by one-half of a 50 mg tablet every 5 days until a maximum of 100 mg per day was achieved approximately 2 weeks after initiation. Tremor was assessed by the Fahn-Tolosa-Marin (FTM) Tremor Rating Scale after one week of primidone administration. A subjective reduction in FTM Part I rating scores from 14 to 8 was also measured at this point in therapy. With respect to adverse events profile, the patient reported mild somnolence after

primidone initiation, but this resolved within one month of treatment. The total daily dose of primidone was increased to 100 mg/day (50 mg BID), and the patient returned to our clinic after approximately one month at this dosage level. The patient reported moderate improvement in tremor on the Clinical Global Impression Scale. Moreover, FTM Part I clinical rating scores improved drastically from 14 to 4. He opted to continue primidone treatment and has done so for 16 weeks without side effects and sustained tremor reduction.

Discussion

Primidone is an antiepileptic that was for many years the drug of choice in the treatment of various seizure disorders. This case report describes one patient with ET who experienced significant improvement in upper-extremity tremor following the administration of primidone. At daily doses of 50–100 mg, the severity of tremor amplitude was reduced by 50% in the worst-affected (right) hand, and the patient experienced marked improvements as assessed by subjective outcome measurements (FTM clinical rating scale). In the present case, the patient reported only mild somnolence on primidone initiation. Mild somnolence is a typical side effect which usually disappears after prolonged exposure, and which in this case resolved within one month, with no detriments to activities of daily living. Dose-limiting qualities of first-line ET treatments are such that the adjunction of primidone to propranolol, or vice versa, may become necessary for reducing tremor amplitude and overall severity.

Questions

1. Which of the following neurologic diseases is most common?
A. Parkinson disease
B. Alzheimer's disease
C. ET
D. Spinocerebellar ataxia

The correct answer is C. Populations studies estimate the prevalence of ET is between 0.4% and 5% (Louis 1998; Benito-Leon 2003).[3]

2. Which of the following medications is considered a first-line agent for treating ET?
A. Alprazolam
B. Metoprolol
C. Clonazepam
D. Propranolol

The correct answer is D. Propranolol is the only medication approved by the US Food and Drug Administration to treat ET. Propranolol, propranolol LA, or primidone should be offered to patients who desire treatment for limb tremor in ET, depending on concurrent medical conditions and potential side effects (Class I studies, Level A).[3]

3. It is estimated that what percentage of patients with ET will not respond favorably to antitremor medication?
A. 10% to 20%
B. 30% to 50%

C. 60% to 75%
D. 0% to 5%

The correct answer is B. A study by Koller et al. (1989) examined the acute and chronic effects of primidone and propranolol and observed a lack of therapeutic effect in this proportion of participants.[3]

4. The use of topiramate (Topamax) for treatment of ET carries what level of recommendation by this AAN guideline?
A. Level A
B. Level B
C. Level C
D. Level U

The correct answer is B. Topiramate should be considered as treatment of limb tremor associated with ET (Class II studies, Level B).[3]

5. Alprazolam, atenolol, gabapentin (monotherapy), and sotalol carry what level of recommendation by this AAN guideline?
A. Level A
B. Level B
C. Level C
D. Level U

The correct answer is B. Atenolol, gabapentin (monotherapy), and sotalol should be considered as treatment of limb tremor associated with ET (Class I studies, Level B). Alprazolam is recommended with caution due to its abuse potential (Class I and II studies, Level B).[3]

6. Nadolol, nimodipine, clonazepam, and botulinum toxin type A carry what level of recommendation by this AAN guideline?
A. Level A
B. Level B
C. Level C
D. Level U

The correct answer is C. Clonazepam, clozapine, nadolol, and nimodipine possibly reduce limb tremor associated with ET (Level C).[3]

Diagnosis Coding
The ICD-9-CM[1] code for essential tremor (ET) is:

333.1 Essential and other specified forms of tremor

During the later visit for evaluation of effects of the Primidone, the complaint of somnolence would be added as a second code as:

780.09 Alteration of consciousness, Other, Somnolence

Evaluation and Management Coding
Assuming the patient had Medicare, the appropriate E&M code for this visit would be 99204, a level 4 new-patient visit.[2] The history and physical are comprehensive, and the medical decision making is moderate complexity.

[1]Practice Management Information Corporation. *International Classification of Diseases*, 9th revision; clinical modification, 6th edition. Los Angeles, CA: Practice Management Information Corporation; 2006.
[2]Centers for Medicare and Medicaid Services. *Evaluation and Management Services Guide*. Baltimore, MD: Centers for Medicare and Medicaid Services; December 2010.
[3]Zesiewicz TA, Elble RJ, Louis ED, et al. Evidence-based guideline update: Treatment of essential tremor: Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology® 2011;77:1752–1755.

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