By Zac Haughn, Associate Editor

Managing Essential Tremor: Tailoring Therapy to Each Patient's Needs

Q ***What is typically your first line therapy for essential tremor? What factors influence the initiation of drug therapy in an ET patient? Do you simply go by what the patient wants or does your recommendation also hinge on factors like age or profession?***

A There was no disagreement among our panelists on how to start a patient on ET therapy. Typically, ET patients are prescribed an anticonvulsant that has demonstrated efficacy in reducing tremor, such as primidone (Mysoline) or topiramate (Topamax), or one of the beta-blockers that is also anti-hypertensive agent, such as propranolol (Inderal). "Treatment generally begins when the tremor begins to interfere with the patient's ability to perform daily activities, or if the tremor is embarrassing to the patient," says Julián Benito-León, MD, PhD.

The choice of medication "depends on the side effect profile of the medication, as well as co-morbid conditions of the patients," says Theresa Zesiewicz, MD. For example, a health care provider would want to take into account whether a patient suffers from cardiac or respiratory problems before initiating an anti-hypertensive, she says. "Other medications that patients are taking need to be taken into account also, as they may interact with medications used for tremor." Younger patients with milder tremor are started on propranolol unless they have a contraindication to beta blockers (e.g., asthma), while older patients with more severe tremor are started on primidone, according to Rodger J. Elble, MD, PhD.

Profession does affect which medication or how much of it one prescribes for tremor, according to Dr. Zesiewicz. "For example, a fair number of dentists come to my practice, asking for relief from tremor that significantly impacts their jobs. This is a very different scenario than a retired person who can live with a tremor," she says. The important thing to let patients know is that in most cases, medication reduces the severity of tremor by about half, she adds. "Very often, we cannot completely 'stop' a tremor; the tremor may become worse with anxiety or somnolence. So it is important to discuss realistic expectations for patients, as well."

Q ***If a patient with essential tremor is not able to handle the side effects of Inderal, what beta blocker would you try next and at what dose? What precautions would be necessary when adding a different drug?***

A This area is slightly more "touch and go" and less defined than the first line therapies. Other β-adrenoceptor antagonists have been used with varying efficacy in the treatment of essential tremor. "Among these agents, atenolol, a selective B-adrenoceptor antagonist, might have anti-tremor efficacy in patients with essential tremor but less than that of the β-adrenoceptor antagonist sotalol or propranolol," Dr. Benito-León says. He adds that Sotalol (75 to 200 mg/day) and another β-adrenoceptor antagonist, nadolol (120 to 240 mg/day), have both been shown to reduce tremor compared with placebo. In general, however, β-adrenoceptor antagonists "share the same side effects and are relatively contraindicated in patients with asthma, diabetes mellitus or atrioventricular block, and absolutely contraindicated in patients with unstable heart failure," Dr. Benito-León says. If a patient with essential tremor is not able to handle the side effects of Inderal, he would use an alternative drug, such as primidone, topiramate, or gabapentin.

Dr. Elble votes for Metoprolol in such cases, under condition, however. "Warn patients that the same side effect may occur with other beta blockers, so if the side effect of propranolol is severe, I would avoid beta blockers," he says.

Q ***When using Topamax, is there any way to minimize the sedating effect? A recent study found that nausea, paresthesia, and concentration/attention difficulty were common side effects. Is this consistent with what you see in your practice? What are pharmacological options for these issues?***

A All three of our panelist agreed patients should start on Topamax at 25mg. "Titrate the daily dosage in 25mg increments as tolerated and as needed, using bid dosing," Dr. Elble recommends. "The paresthesias often resolve with time." Memory and concentration difficulties are common, and these problems and lack of efficacy are the most common reasons for stopping the drugs, he says. "I would stop the drug if there is persistent excessive sedation; most these patients also have cognitive side effects."

The side effects of topirimate can become very worrisome to doctors and patients. "I published a report on two of my patients who developed hallucinations while taking it," Dr. Zesiewicz says. A study by Ondo et al found that Topamax effectively reduced tremor at a fairly low dose, she says. "I start patients

with Topamax 25mg twice a day for one week and titrate slowly each week to reach the desired effect. Patients often have a favorable response at 75 to 100mg daily."

Q ***One study found[1] that ET patients were twice as likely to report being depressed and three times as likely to be on antidepressant therapy, compared to controls. What needs to be taken into account when starting an ET patient on an antidepressant? What are your first line options?***

A Dr. Benito-León suggests physicians be open to alprazolam in such cases. At a "dose ranging from 0.75 to 2.75mg daily it is more effective than placebo at reducing tremor." In addition, it has a mild antidepressant effect. He says it could be a good option and adds other medications to consider would include escitalopram or citalopram.

"Depression and migraine are common comorbidities. An occasional patient will experience increased tremor," Dr. Elble says. "If so, I try mirtazepine. If the patient has migraine, I try propranolol or topiramate because these drugs are good for migraine prophylaxis." **PN**

1. Louis ED, Benito-León J, et al. Self-reported depression and anti-depressant medication use in essential tremor: cross-sectional and prospective analyses in a population-based study. Eur J Neurol. 2007 Oct;14(10):1138-46.

Julián Benito-León, MD, PhD is in the Department of Neurology at University Hospital "12 de Octubre" in Madrid, Spain.

Rodger J. Elble, MD, PhD is Professor and Chair of Neurology at Southern Illinois U. School of Medicine.

Theresa Zesiewicz, MD is Professor of Neurology at the University of South Florida.

PRACTICAL PEARLS

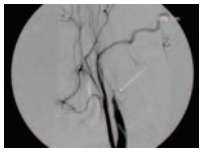
Side effects like low body temperature, headache, nightmares and worsening of depression are reported with melatonin. Caution is advised in patients with epilepsy, who are taking warfarin, have autoimmune or endocrine diseases, or are pregnant or breastfeeding. Varying levels of quality, purity, and quantity of active ingredient calls melatonin supplements into question. p. 30

When evaluating patients with cerebellar motor disorders and finding behavioral and cognitive impairment, we should not jump to the conclusion the patient must have cerebral pathology as well. Remember, patients with Alzheimer's and other dementia can have cerebellar and brain stem strokes, which can worsen their dementia without concluding multiple cerebral strokes have also occurred. p. 42

Malignant hyperthermia (MH) is a rare and life-threatening neuromuscular condition, usually affecting young and previously asymptomatic adults undergoing general anesthesia. The neurologist should take a lead in identifying patients and families at risk for MH, perform appropriate diagnostic testing including molecular genetic testing if possible, and raise the awareness about this rare but often fatal condition. p. 18

Studies have shown that up to two-thirds of people do not report CAM use to their doctor. Moreover, many physicians are unaware of the potential problems that can arise from use of these therapies. A careful history should therefore include detailed questions regarding CAM use. p. 11

Pregnancy seems to have a positive benefit on the development of disability in women who have been pregnant. A five-year, prospective study compared the rate of progression in disability between childless women, women who had onset of MS after childbirth, and women who had onset before or during their pregnancy...The rates of disability increased over the five years most rapidly in the group that was childless. p. 39



Although anticoagulation is the widely-advocated treatment for ICAD, it is still debated whether this approach is superior to antiplatelet agents. Unfortunately, evidence from randomized trials on the efficacy of either therapeutic approach is missing. In spite of the controversy, physicians still have to decide whether an individual with ICAD should receive immediate anticoagulation or antiplatelet agents in order to prevent cerebral infarction. p. 25

When asked what they liked about their job, the number one answer for nurses was "The physicians I work with." This was followed by "My colleagues," "The work is interesting," "I feel appreciated," "My best skills are respected and utilized," and "I feel like a member of the team." All of these responses were ranked higher than "Hours," "Pay," and "Benefits." p. 9

Expsoure to light reduced cognitive deficits by five percent among AD patients; that is, there was an increase in the MMSE score of 3.5 points. The light also reduced depression by 19 percent and attenuated functional limitations by 53 percent...Melatonin had no effect on the depression rating, but adversely affected care-giving ratings of withdrawn behavior and mood. However, it reduced sleep onset latency by 19 percent and increased the total sleep duration by six percent. When melatonin was combined with bright light it reduced agitated behavior by nine percent, improved sleep efficiency by 3.5 percent and reduced nocturnal restless by 10 percent. p. 43