AAN Summary of Evidence-based Guideline for CLINICIANS

UPDATE: TREATMENT OF ESSENTIAL TREMOR

This is a summary of the American Academy of Neurology (AAN) guideline update regarding treatment of essential tremor (ET).

Please refer to the full 2005 guideline and 2011 update at www.aan.com for more information, including definitions of the classifications of evidence and recommendations.

Pharmacologic Treatments

What are the safety, tolerability, and efficacy of pharmacologic agents in treating ET?

Propranolol, propranolol long-acting, or primidone should be offered to patients who desire treatment for limb tremor in ET, depending on concurrent medical conditions and potential side effects (**Level A**[†]).
Trazodone is *not* recommended for treatment of limb tremor in ET (**Level A**).
Atenolol, gabapentin (monotherapy), sotalol, and topiramate should be considered as treatment of limb tremor associated with ET (**Level B**).
Alprazolam is recommended with caution due to its abuse potential (**Level B**).
Propranolol should be considered as treatment of head tremor in patients with ET (**Level B**).
Acetazolamide, isoniazid, and pindolol are *not* recommended for treatment of limb tremor in ET (**Level B**).
Nadolol and nimodipine may be considered when treating limb tremor in patients with ET (**Level C**).
Clonazepam should be used with caution due to its abuse potential and possible withdrawal symptoms (**Level C**).
Methazolamide, mirtazapine, nifedipine, and verapamil are *not* recommended for treatment of limb tremor in ET (**Level C**).
There is insufficient evidence to make recommendations regarding the use of amantadine, clonidine, gabapentin (adjunct therapy), glutethimide, L-tryptophan/pyridoxine, metoprolol, nicardipine, olanzapine, phenobarbital, quetiapine, and theophylline in the treatment of limb tremor in ET (**Level U**).

New/changed recommendations since the 1995 guideline

Moderate evidence	Levetiracetam and 3,4-diaminopyridine should *not* be considered for treatment of limb tremor in ET (**Level B**).
Weak evidence	Clinicians may choose *not* to consider flunarizine for treatment of limb tremor in ET (**Level C**).
Insufficient evidence	The evidence is insufficient to make recommendations regarding the use of pregabalin, zonisamide, or clozapine (**Level U**).

Which drug should be used for initial treatment of ET?

Either primidone or propranolol may be used as initial therapy to treat limb tremor in ET **(Level B**).

In patients with ET, is combined treatment with primidone and propranolol superior to monotherapy?

Primidone and propranolol may be used in combination to treat limb tremor when monotherapy does not sufficiently reduce tremor (**Level B**).

In patients with ET, is there evidence for sustained benefit of pharmacologic treatment?

The dosages of propranolol and primidone may need to be increased by 12 months of therapy when treating limb tremor in ET (**Level C**).

Do patients with ET benefit from chemodenervation with botulinum toxin type A or B?

Botulinum toxin type A injections for limb, head, and voice tremor associated with ET may be considered in medically refractory cases (**Level C** for limb, head, and voice tremor).

Nonpharmacologic Treatments

Should thalamotomy or deep brain stimulation (DBS) of the thalamus be the procedure of choice in patients with medically refractory ET?

DBS has fewer adverse events than thalamotomy (**Level B**). However, the decision to use either procedure depends on each patient's circumstances and risk for intraoperative complications compared to feasibility of stimulator monitoring and adjustments.

What are the indications for bilateral vs. unilateral surgical procedures in ET? What is the efficacy of thalamotomy in treating contralateral limb tremor in patients with ET?

Unilateral thalamotomy may be used to treat limb tremor in ET that is refractory to medical management (**Level C**), but bilateral thalamotomy is not recommended due to adverse side effects (**Level C**).

Bilateral DBS is necessary to suppress tremor in both upper limbs, but there are insufficient data regarding the risk-benefit ratio of bilateral vs. unilateral DBS in the treatment of limb tremor (**Level U**). Similarly, there are insufficient data to recommend bilateral or unilateral DBS for head and voice tremors. Side effects are more frequent with bilateral DBS, and bilateral thalamotomy is not recommended.

What is the efficacy of DBS of the thalamus in treating tremor in patients with refractory ET?

DBS of the ventral intermediate thalamic nucleus may be used to treat medically refractory limb tremor in ET (**Level C**).

There is insufficient evidence to make recommendations regarding the use of thalamic DBS for head or voice tremor (**Level U**).

Does gamma knife thalamotomy effectively reduce ET?

There is insufficient evidence to make recommendations regarding the use of gamma knife thalamotomy in the treatment of ET (**Level U**).

Clinical Context for Surgical Treatments

No high-quality, long-term studies exist regarding the efficacy and safety of these interventions for ET.

Clinical Context

Flunarizine use may result in development of movement disorders, including akathisia, dyskinesia, dystonia, and parkinsonism. As an atypical neuroleptic agent, olanzapine can induce parkinsonism. A review of 11 published studies of olanzapine use in patients with Parkinson disease found reports of worsening parkinsonism in 64 of 145 patients (44%). However, this side effect was not observed in the study of patients with ET.

ET is a common movement disorder, and Class I evidence supports the successful use of primidone and propranolol in ET treatment. However, not all patients improve on or tolerate these medications. A survey of 223 patients in a clinical database revealed that 70.9% had taken primidone or propranolol, and 56.3% had discontinued one or both medications. Thus, these first-line medications for ET clearly fail to meet the needs of many patients.

Based on an AAN guideline endorsed by the International Essential Tremor Foundation

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