Guidelines for management of essential tremor

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Essential tremor (ET) is a common movement disorder, and approximately 50% of the cases are inherited as an autosomal dominant trait.[1] The incidence of ET increases with age, may manifest at any age (childhood to adulthood), and those with a positive family history have an earlier age of onset.[2] The tremor involves mainly the upper limbs distally and is postural or kinetic type. The less common parts involved with tremor are the head, lower limbs, voice, tongue, face, and the trunk. The tremor amplitude increases with time, and patients experience difficulty in writing, eating, holding objects and doing fine motor tasks, dressing, and speaking.[3] Although ET usually does not reduce life expectancy or cause other symptoms, many patients have severe psychosocial disability.[3] Tremor often increases with anxiety, stress, and in situations involving interaction with others. Patients with head and voice tremor often suffer severe embarrassments, and may develop depression.

ET should be differentiated from the other types of tremors, especially tremor of Parkinson's disease, tremor associated with hyperthyroidism, and dystonic tremor of head in patients with isolated head tremor. Once a diagnosis is made, the severity of functional and psychosocial disabilities should be assessed by objective scales, which will help to determine the need for pharmacotherapy.

The management of a patient with ET includes (a) behavioral techniques and physical therapy, (b) medical therapy, and (c) surgical treatment. The patient should be explained about the disease, the long-term outcome, and what the therapies can achieve. All therapies are essentially symptomatic and will not cure or change the course of the disease. If there is minimal functional disability, the patient need not take treatment. Even if the tremor is controlled by medical therapy, stress and anxiety can increase the symptoms. An outline of the management of ET is given in Figure 1.

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Behavioral Techniques and Physical Therapy

Not all patients with ET will need treatment with drugs. Treatment depends on the severity of tremor, the body part affected, and the occupation of the patients. It is also determined by the degree of social disability. In patients with less disabling tremor, certain behavioral techniques and physical therapy may be useful. These include relaxation therapies and reducing emotional stress, using the less disabled hand to write or eat, using wrist weights[2] and minimizing exposure to tremorogenic foods (eg, caffeine) and drugs (eg, sympathomimetics).

Medical Treatment

Treatment schedules

When it is decided to start medical treatment, it can be of 2 types:

1. Intermittent treatment: ***On an as-needed or scheduled basis.*** This is recommended when the patient is distressed mainly in social gatherings or prior to an important social activity. A half to 2 tablets of propranolol (20 mg) can be administered 30 min to 1 h before a social activity or the anxiety-provoking event, which increases tremor. Alternatively, a benzodiazepine, such as lorazepam or clonazepam can be administered prophylactically. However, as the benzodiazepines can cause central nervous system adverse events and also have abuse potential, they need to be administered judiciously. Although routine use of alcohol is not recommended, in patients with alcohol responsive tremors, judicial use of a small amount of alcohol prior to select social activities, such as social dinner, can be considered.
2. As long-term suppressive therapy: In patients who need long-term therapy, the following drugs have proved to be useful with varied efficacy and levels of recommendations, based on the class of evidence.

Drugs of choice

β-Blockers, most commonly propranolol, and primidone are the drugs of choice for treatment of ET. Both these agents have level

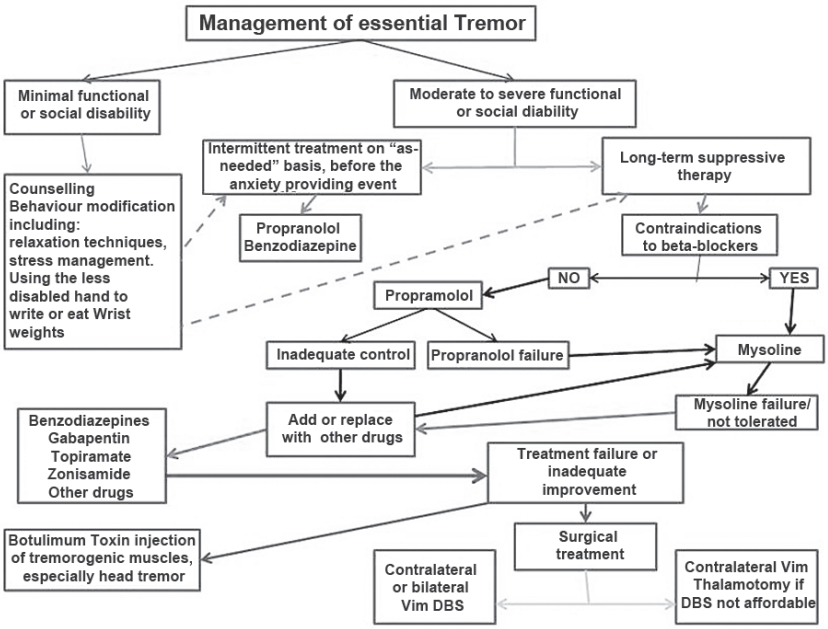

Figure 1: A flow chart showing the steps in the management of essential tremor

A recommendation, and either can be used for initial treatment of ET,[4] depending on the concurrent medical conditions, and potential side effects.

Propranolol (β-2 blocker)

Treatment should be initiated at 10 mg once daily and gradually titrated (eg, every 3–7 days) to 20 mg twice daily. Elderly individuals may need a lower dose (eg, 10 mg twice daily), while for those who are tolerating well, propranolol can be increased up to 240 mg/day in divided doses. Improvement occurs in approximately 50%–60% of the patients, the greatest improvement being for hand tremor, and the least for head or voice tremor. Long-acting preparations of propranolol also have a similar efficacy. Ten to 15 percent of the responders may develop tolerance after a year of treatment.[5] Side effects include light headedness, fatigue, impotence, bradycardia, and reduced blood pressure. Relative contraindications to propranolol are severe heart failure, conduction blocks, hyperactive airway disease, depression, and diabetes.

Primidone

The efficacy of primidone for managing ET appears to be similar to propranolol[5] and it can be an initial therapy, although most often this is started after the failure of propranolol to control ET satisfactorily. Currently, this drug is not easily available in India. The treatment is initiated at the lowest possible dose and gradually titrated up to avoid side effects, which often appear. When a 50 mg tablet or an oral suspension preparation (50 mg/mL) is available (not available in India), it can be started at 12.5 mg at bedtime and slowly titrated upward (increments by 12.5 mg every week) to the dose when desirable tremor control is achieved without significant side effects. Most patients achieve an optimal tremor control at 250 mg/day, although higher doses up to 750–1000 mg/day may sometimes be required. When a patient requires a lower dose, once daily dosing may be adequate; with higher dosage, the drug should be given in 3 divided dosages. In India, since only 250 mg tablets are available, the treatment is usually started with one-quarter of a tablet (or even smaller if feasible) at bedtime, and gradually increased by one-quarter every week, till the tremor control is achieved (the final dose may be given in 3 divided dosages). When the patient cannot tolerate any increment of dosage, he may continue the previous dosage for a longer time, and then try further increment of dosage.

The most common side effect of primidone is sedation and drowsiness, and the other common side effects being nausea, vomiting, dizziness, ataxia, confusion, vertigo, and acute toxic reaction. Patients on primidone should have a complete blood count before starting the treatment and again every 6–12 months, as it has been reported, although rarely, to cause red cell hypoplasia, aplasia, agranulocytosis, and megaloblastic anemia. It is contraindicated during pregnancy, lactation, and in patients having porphyria and hepatic and renal dysfunctions.

Combination therapy

When monotherapy with propranolol or primidone does not adequately control limb tremor, these 2 drugs can be used in combination. It has been shown that there may be an added beneficial effect without an increase in side effects.[4]

Other drugs

The following drugs have lower level (level B or C) recommendations for treating ET, and should be tried (add on or monotherapy) in patients not adequately responding to propranolol or primidone, or when there are prominent side effects:

Benzodiazepines

This group of drugs, which probably augments GABA activity, can be used as add-on treatment for ET. Alprazolam (0.125–3 mg/day), clonazepam (0.5–6 mg/day), lorazepam (1–10 mg/

day), and diazepam (1–10 mg/day) can be considered in patients with significant worsening of tremor due to anxiety or emotional stress. Clonazepam may be particularly useful for treatment of orthostatic tremor, a rare variant of ET.[6] The drugs should be used with caution because of their abuse potential, side effects of drowsiness and fatigue, and possible withdrawal symptoms following abrupt discontinuance.

Gabapentin

Gabapentin (structure similar to GABA) can be used as a monotherapy or as an add-on therapy for treatment of ET.[7-9] It is started at 300 mg 3 times daily, and titrated up to 1200–1800 mg/day. The drug is usually well tolerated with few side effects (sedation, irritability, ataxia, weight gain).

Topiramate

Topiramate (blocks sodium channels and potentiates GABA activity) has been shown to be effective in reducing ET (monotherapy or add-on therapy).[10-12] It is started at 25–50 mg at bedtime and titrated up to 400 mg/day. Side effects include suppression of appetite, weight loss, and paresthesias. Further studies are required to prove its efficacy in ET.

Zonisamide

Zonisamide (acts on sodium and calcium channels) has been reported to be useful in ET, especially for tremors of voice, face, tongue, and head.[13] It is initiated at 25 mg at bedtime and gradually increased to 200 mg/day. Side effects include sleepiness, fatigue, headache, and paresthesias. The drug can be used as monotherapy or add-on therapy of ET in those who have unsatisfactory response to other antitremor medications at maximally tolerated dosage. Further studies are required to determine the efficacy of zonisamide in ET.

Other drugs

There are reports of possible beneficial effects of pregabalin (starting at 50 mg/day and escalated to 600 mg/day), atenolol (50-150 mg/day) , sotalol (75–200 mg/day), nadolol (120–240 mg/day), clozapine (6–75 mg/day), and nimodipine (120 mg/day) in ET. Clozapine is recommended only for refractory cases of limb tremor in ET[14,15] and patients should be monitored for agranulocytosis. Further studies are required to prove the efficacy of these drugs.

Botulinum Toxin

In medically refractory cases of ET, injections of Botulinum Toxin-A in the tremorogenic muscles (preferably under electromyographic guidance for selecting the muscles) may be useful[4] . The injection has been shown to be useful for limb, head, and voice tremor.[16-20] Side effects include temporary weakness of the injected muscles and breathlessness, dysphagia, and hoarseness following treatment for voice tremor. Botulinum toxin injection should be performed only by a trained and experienced neurologist.

Surgical Treatment

Surgical treatment for ET is reserved for those selected patients who have severe tremor not adequately controlled by medical therapy. Contralateral thalamotomy (VIM nucleus) or deep brain stimulation (DBS) of the thalamus are highly effective in reducing tremor.[21-22] In India, the choice between thalamotomy and DBS is primarily dictated by the availability of expertise and the cost of DBS. Bilateral thalamotomy is not recommended due to its adverse side effects. Therefore, in those who cannot afford DBS, unilateral thalamotomy contralateral to the most severely affected side is recommended. In patients who can afford DBS, bilateral DBS is recommended to suppress tremor of both sides. There is contradictory evidence that bilateral DBS may be useful for suppressing head and voice tremor. Side effects are more frequent with bilateral DBS.

In summary, ET is a disorder, which can lead to a significant morbidity in some patients, especially functional disability. The approach to management should be guided by the severity of tremor, the parts of the body involved, occupation of the patient, and physical and social disability.

References

1. Findley LJ, Koller WC. Definitions and behavioral classifications. In: Findley LJ, Koller WC. editors. Handbook of Tremor Disorders. New York, NY: Marcel Dekker; 1995. p. 1-5.
2. Chen JJ, Swope DM. Essential tremor. J Pharma Pract 2007;20:458.
3. Koller WC, Biary N, Cone S. Disability in essential tremor: Effect of treatment. Neurology 1986;36:1001-4.
4. Zesiewicz TA, Elble R, Louis ED, Hauser RA, Sullivan KL, Dewey RB Jr, et al. Practice Parameter: Therapies for essential tremor Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 2005;64:2008-20.
5. Koller WC, Vetere-Overfield B. Acute and chronic effects of propranolol and primidone in essential tremor. Neurology 1989;39:1587-8.
6. Papa SM, Gershanik OS. Orthostatic tremor: An essential tremor variant. Mov Disord 1988;3:97-108.
7. Pahwa R, Lyons K, Hubble JP, Busenbark K, Rienerth JD, Pahwa A, *et al*. Double-blind controlled trial of gabapentin in essential tremor. Mov Disord 1998;13:465-7.
8. Gironell A, Kulisevsky J, Barbanoj M, López-Villegas D, Hernández G, Pascual-Sedano B. A randomized placebo-controlled comparative trial of gabapentin and propranolol in essential tremor. Arch Neurol 1999;56:475-80.
9. Ondo W, Hunter C, Vuong KD, Schwartz K, Jankovic J. Gabapentin for essential tremor: A multiple-dose, doubleblind, placebo-controlled trial. Mov Disord 2000;15:678-82.
10. Connor GS. A double-blind placebo-controlled trial of topiramte treatment for essential tremor. Neurology 2002;59:132-4.
11. Ondo WG, Jankovic J, Connor GS, Pahwa R, Elble R, Stacy MA, *et al*. Topiramate in essential tremor: A double-blind, placebo-controlled trial. Neurology 2006;66:672-7.
12. Frima N, Grunewald RA. A double-blind, placebo controlled, crossover trial of topiramate in essential tremor. Clin Neuropharmacol 2006;29:94-6.
13. Morita S, Miwa H, Kondo T. Effect of zonisamide on essential tremor: A pilot crossover study in comparison with arotinolol. Parkinsonism Relat Disord 2005;11:101-3.
14. Ceravolo R, Salvetti S, Piccini P, Lucetti C, Gambaccini G, Bonuccelli U. Acute and chronic effects of clozapine in essential tremor. Mov Disord 1999;14:468-72.
15. Pakkenberg H, Pakkenberg B. Clozapine in the treatment of tremor. Acta Neurol Scand 1986;73:295-7.
16. Brin MF, Lyons KE, Doucette J, Adler CH, Caviness JN, Comella CL, *et al*. A randomized, double masked, controlled trial of botulinum toxin type A in essential hand tremor. Neurology 2001;56:1523-8.

17. Pahwa R, Busenbark K, Swanson-Hyland EF, Dubinsky RM, Hubble JP, Gray C, *et al*. Botulinum toxin treatment of essential head tremor. Neurology 1995;45:822-4.
18. Wissel J, Masuhr F, Schelosky L. Quantitative assessment of botulinum toxin treatment in 43 patients with head tremor. Mov Disord 1997;12:722-5.
19. Warrick P, Dromey C, Irish JC, Durkin L, Pakiam A, Lang A. Botulinum toxin for essential tremor of the voice with multiple anatomical sites of tremor: A crossover design study of unilateral versus bilateral injection. Laryngoscope 2000;110:1366-74.
20. Hertegard S, Granqvist S, Lindestad PA. Botulinum toxin injections for essential voice tremor. Ann Otol Rhinol Larnygol 2000;109:204-9.
21. Zirh A, Reich SG, Dougherty PM, Lenz FA. Stereotactic thalamotomy in the treatment of essential tremor of the upper extremity: Reassessment including a blinded measure of outcome. J Neurol Neurosurg Psychiatry 1999;66:772-5.
22. Pahwa R, Lyons KL, Wilkinson SB, Carpenter MA, Tröster AI, Searl JP, *et al*. Bilateral thalamic stimulation for the treatment of essential tremor. Neurology 1999;53:1447-50.

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