Movement Disorder Updates

Essential Tremor
Parkinson's disease
Restless Leg Syndrome

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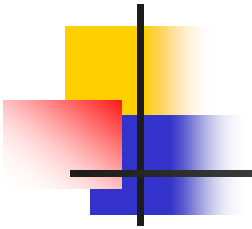


Essential Tremor (ET)

Clinical Features

- Frequently runs in families
- Most often affects hands and arms (severity can be asymmetric)
- Can also affect the head, voice, chin, trunk, and legs
- Becomes apparent in arms when held outstretched (postural)
- Typically increases at the very end of goal-directed movements such as eating or drinking from a glass (action or kinetic)
- Typically relieved by small amounts of alcohol
- Can worsen with age

DDx: Parkinson's disease

- Differentiation from classic resting tremor straightforward but…
  - some patients with PD also have postural-action tremor
  - some patients with severe ET may have rest component
- Head tremor more likely to be ET whereas jaw PD
- DAT scan can help differentiate ET and PD

DDx: Cervical Dystonia

- Observe position of head at rest while patient has eyes closed (patients with cervical dystonia will generally exhibit rotation or flexion to one side)
- Dystonic “tremor” will be irregular

Treatment Summary

- When disability exists, drug treatment should be attempted, unless contraindicated
- Non-responders to oral medications may respond to botulinum toxin type A injections (more evidence to support improvement in head tremor)
- Surgical options may be appropriate for severe tremor refractory to conservative management

Medications for ET

- Propranolol and primidone have similar effectiveness
- Estimated that at least 30% of patients will not respond to either agent
- May be used in combination and combined use may be more effective than either drug alone
- May require increased dosages by 12 months of therapy

Propranolol

- Only about 50% of patients respond
- Relative contraindications include heart block and bronchospastic disease
- Use can be limited by chronic side effects such as lightheadedness, fatigue, impotence and bradycardia

Propranolol Dosage Information

- Used at dosages of 60-320 mg/day to reduce limb tremor (probably also reduces head tremor but data are limited)
- Max tremor suppression more likely to occur between 160 and 320 (mean dosage in clinical studies =185.2 mg)
- Long acting form also effective and more convenient
- Single doses can be used in anticipation of social situations that are likely to exacerbate tremor

Primidone

- Begin at a dosage of 12.5 to 25 mg q HS and slowly titrate over several weeks as necessary and tolerated up to 750 mg/day (consider dividing doses at higher dosages)

- Use can be limited by side effects including sedation, fatigue, nausea, vomiting, ataxia, dizziness, unsteadiness, and confusion

Other Beta Blockers

- Not as much evidence to support their use as for propranolol
- Can consider a selective beta adrenergic blocker for use in patients who cannot take propranolol (e.g., asthma)
- Would try primidone first
- Atenolol > Metoprolol

Second Line Medications

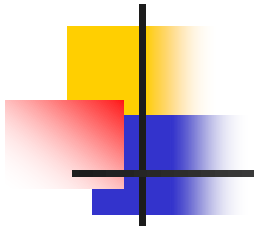
- Gabapentin
  - 1200 mg/day reduced tremor compared with placebo
  - Start with 100 mg TID in elderly
- Topiramate
  - 300-400 mg/day reduced tremor compared with placebo
  - Start with 25 mg daily, then increase weekly by 25-50 mg/day
  - Side effects are common and include nausea, paresthesia and decreased concentration

Botulinum Toxin Muscle Injections

- Botulinum toxin type A injections can be considered for patients with medication-refractory head tremor
- Hand tremor
  - Reduced tremor amplitude by 30%
  - No improvement in functional ratings
  - Finger weakness usually unacceptable to the patient
- Dependent on physician's expertise

Surgical Management of ET

- Deep Brain Stimulation (thalamus)
- Stereotactic thalamotomy



Parkinson’s Disease

When to start medication in PD

- Currently no intervention *proven* to slow disease progression
- May decide to wait until symptomatic treatment is required (which is subjective and varies quite a bit among patients)
- Consider participation in a clinical trial (FOX trial finder)
- Consider rasagiline, which *may* have disease modifying potential

Medications used to treat PD motor features

- Carbidopa/levodopa (often referred to by brand name Sinemet)
- COMT inhibitors (entacapone)
- Dopamine agonists (pramipexole, ropinirole, rotigitine)
- MAO-B inhibitors (selegiline, rasagiline)
- Amantadine

Which medication to start with?

- There are many approaches and patient-specific factors must be considered (e.g., age, cognitive status)
- Carbidopa/levodopa is often the initial treatment of choice as it is the most effective and generally well-tolerated

Motor Fluctuations

- Wearing off of medication prior to next schedule dose
- Dyskinesias (“peak dose”, wiggling movements)
- Patients may fluctuate between
  - “off” (parkinsonian)
  - “on” (good medication effect)
  - “on with dyskinesias” (+/- bothersome)
- Generally start after several years of dopaminergic treatment and disease progression

Medication adjustments for fluctuations

- Sinemet CR is erratically absorbed and doesn't provide continuous LD
- Can lower dosage and increase frequency of CD/LD dosing
- Can add a COMT inhibitor, dopamine agonist or MAOB inhibitor
- Consider adding amantadine to reduce dyskinesias
- Can now consider new levodopa formulation ("Rytary") in an effort to decrease off time
- Can now consider intestinal levodopa gel (requires feeding tube) to lessen fluctuations

General Indications for DBS Surgery

- Idiopathic PD (not atypical parkinsonism)
- Excellent response to levodopa but has developed motor complications
  OR
- Treatment refractory tremor
- No unstable psychiatric condition
- Good cognition
- No significant gait/balance problems when “on”
- Healthy enough to undergo surgery

Restless Leg Syndrome (RLS)

Diagnostic Criteria for RLS

- 1. An urge to move the legs usually but not always accompanied by, or felt to be caused by, an uncomfortable and unpleasant sensations in the legs.
- 2. The urge to move the legs and any accompanying unpleasant sensations begin or worsen during periods of rest or inactivity, such as lying down or sitting.
- 3. The urge to move the legs and any accompanying unpleasant sensations are partially or totally relieved by movement, such as walking or stretching, at least as long as the activity continues.
- 4. The urge to move the legs and any accompanying unpleasant sensations during rest or inactivity only occur or are worse in the evening or night than during the day.
- 5. The occurrence of the above features are not solely accounted for as symptoms primary to another medical or a behavioral condition (e.g., myalgia, venous stasis, leg edema, arthritis, leg cramps, positional discomfort, habitual foot tapping).

Associated Conditions and Alternative Dx's

- Associated conditions
  - low systemic iron stores
  - pregnancy
  - renal disease
  - diabetes
  - neuropathy

- Conditions with which RLS may be confused
  - leg cramps
  - neuropathy
  - akathisia
  - periodic limb movements of sleep (PLMS)

Evaluations after making dx of RLS

- Check Ferritin Level
  - Iron supplementation if serum ferritin levels <45–75 μg/L
  - Aim for serum ferritin levels > 75

- Review current medications and substance use for agents that can worsen RLS symptoms
  - dopamine-blocking antiemetics
  - centrally acting antihistamines
  - antipsychotics
  - alcohol, caffeine

Treatment of RLS

- Consider in patients with moderate–severe RLS and for those with intermittent, bothersome symptoms

- Medications:
  - alpha 2 delta calcium channel ligands (e.g., gabapentin)
  - dopamine agonists (best as prn given risk of augmentation)
  - Benzodiazepines, opiates are second line therapies

References and suggested readings

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