

## Treatment of Peripheral Neuropathy in the Older Patient

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## Neuropathy Overview

- Neuropathy prevalence increases with age
- Diminished ankle reflexes and decreased foot/ankle sensation should not be dismissed
- Neuropathy symptoms and signs are significant predictors of adverse outcomes in older adults
- The approach to neuropathy must include evaluation for a treatable cause
- Addressing risk of falls can impact outcome in neuropathy patients

## Neuropathy Descriptors

- Hereditary versus Acquired
- 'Distal/symmetric' versus 'Multifocal'
- 'Motor' versus 'Sensory' versus 'Mixed'
- 'Axon loss' versus 'Demyelinating'
- 'Large fiber' versus 'Small fiber'

## Most Common Neuropathy

- Acquired
- Distal/symmetric
- Sensory > Motor
- Axon loss
- Small fiber > Large Fiber

## Neuropathy Symptoms

- Sensory changes in the feet
  - “Numb toes,” “Dead, wooden, tight feet”
  - “Like my socks are rolled up in the end of my shoe”
- Pain (including allodynia)
  - “Tingling, electrical, sharp”
  - “Increases at night”
- Cramps/Stiffness
- Autonomic symptoms
  - Dizziness on standing, Impotence, Dry eyes, Dry mouth
- Balance problems (sensory ataxia)
- Increasing falls (particularly in a dark room)

## Neuropathy Exam Findings

- Loss of pinprick sensation
- Loss of vibration sense
- Decreased proprioception
- Distal muscle atrophy
- Trouble hopping
- Broad based gait
- Romberg sign
- Orthostatic hypotension
- Abnormal sweating

## Impact of Neuropathy

- Functional decline
- Reduce quality of living
- Social isolation
- Increased risk of 'overmedication'
- Increased risk of hip fractures
- Increased risk of hospitalization

## Treatment Approach

- Identification of a treatable underlying cause (or causes)
- Medical treatment for pain
- Minimizing risk of falls

## Causes in Older Patients

- Diabetes mellitus
- Nutritional: B12 Deficiency
- Other deficiencies (e.g., Folate, Copper)
- Malignancies/Monoclonal protein-associated
- Medications (e.g., Chemotherapy)
- Autoimmune (e.g., Sjogrens, RA)
- Infections (e.g., HIV, Lyme)
- Toxins (e.g., Heavy metals)
- Last but not least common: "Idiopathic"

## Recommended Testing

- *Fasting glucose* tolerance testing, 2 hour
- *Serum protein electrophoresis with IFE*
- *Vitamin B12*, MMA, copper, folate
- Fasting lipid panel (triglycerides)
- Selected patients:
  - TSH, T3, T4
  - Vitamin B6, Vitamin E
  - HIV, Lyme IgM/IgG, RPR, Hep B/C serology
  - ANA, SSA, SSB, RF, ANCA, cryoglobulins
  - Paraneoplastic antibodies (anti-Hu)
  - Heavy metals, 24 hour urine

## Treating the "Treatable Causes": General Principles

- Treatment of the cause can halt progression of neuropathy symptoms
- Earlier treatment of underlying cause increases the odds of recovery
- More "severe" neuropathy reduces the odds of recovery
- Most patients will benefit from the addition of symptomatic treatment

## Treatable Cause: Diabetes

- Most common treatable cause
- Found in 40 - 50% of neuropathy patients age 65 - 75 years
- Early impaired glycemic control is associated with neuropathy (OGTT)
- Neuropathy often precedes other complications in diabetes
- Glycemic control can limit progression reduce neuropathy symptoms

## Treatment of Neuropathic Pain

- Neuropathic pain must be addressed
- Patients may find meditation and staying active helpful, but many require medication
- Age-related changes in absorption and clearance, as well as polypharmacy impact drug selection
- Most drug studies to date do not include a significant portion of patients over age 65
- Treatment “success” in most clinical trials is a reduction in pain by 50% (not complete relief)

## Treatment of Neuropathic Pain

- First line
  - Gabapentinoids (gabapentin, pregabalin)
  - Tricyclic antidepressants (amitriptyline, nortriptyline)
  - Topical lidocaine (for PHN)
- Second line
  - SNRIs (venlafaxine, duloxetine)
  - Tramadol
  - Alternative therapies: Alpha-lipoic acid, L-carnitine
- Third line
  - Opioids

## Neuropathic Pain: Gabapentinoids

- Renal elimination (Caution in HD patients)
- Side effects: dizziness, somnolence, edema
- Few drug interactions (except CNS depressants)
- Gabapentin
  - Start 300 mg at bedtime
  - Increase to 300 mg tid, further increase as tolerated
  - Maximum dose: 3600mg /day
- Pregabalin
  - Start 75 mg bid (dose is generally ineffective, except PHN)
  - Maximum dose: 600mg /day

## Neuropathic Pain: TCAs

- Hepatic metabolism
- Side effects: cognitive impairment, cardiac conduction block, anticholinergic (constipation, urinary retention, dry mouth)
- Reported increased risk of sudden cardiac death with > 100 mg/day of amitriptyline (or equivalent)
- Consider obtaining a baseline ECG prior to use
- Amitriptyline: Start 10 mg at bedtime, increase weekly as tolerated (max: 100 mg)
- Nortriptyline: Start 10 mg at bedtime, increase weekly as tolerated (max: 100 mg)

## Neuropathic Pain: Topicals

- Lidocaine topical
  - Available as a 5% patch
  - Not thoroughly tested, but thought effective for focal neuropathic pain, particularly PHN
  - Minor skin irritation is the only reported side effect
  - No significant systemic absorption
- Capsaicin topical
  - Application initially causes burning
  - Multiple daily applications required
  - Accidental contact with eyes or mucous membranes can be quite painful/distressing
  - Overall, NOT recommended for older adults

## Neuropathic Pain: SNRIs

- General agreement that SNRIs are safer than TCAs and are a better option in cardiac disease
- Side effects: Somnolence, dizziness, gastric pain/nausea
- Risk of SIADH may be increased in older adults
- Baseline sodium and reassessment while taking these medications should be considered
- Venlafaxine
  - Start ER 37.5 mg/day for 1 week, increase to 75 mg daily as tolerated (max: 225 mg/day)
  - Benefit may take up to 6 weeks
- Duloxetine
  - Start 30 mg/day for 1 week, increase to 60 mg daily as tolerated

## Neuropathic Pain: Alternative meds

- Alpha lipoic acid
  - Potent antioxidant
  - Trials in patients with painful diabetic neuropathy confirmed efficacy
  - 600 mg daily is optimal
  - Side effects with higher doses included nausea, vomiting, vertigo, and hypoglycemia
- Acetyl-L-carnitine
  - Also effective in painful diabetic neuropathy at a dose of 1000 mg tid
  - Side effects include hypertension, headache, dizziness, and GI symptoms

## Neuropathic Pain: Tramadol

- Dual mechanism (weak M-opioid and SSRI)
- Suggest a trial of 50 mg daily to ensure tolerability
- Can increase to 50 mg q 6 hours as needed (max dose: 300 mg/day)
- Side effects: Anticholinergic, seizures
- Not recommended for use with other SSRIs

## Neuropathic Pain: Opioids

- Oxycodone, oral morphine, and transdermal fentanyl are effective for chronic neuropathic pain
- For patients who have failed other therapies, judicious use of opioids can improve quality of life
- Side effects: constipation, nausea, drowsiness, and loss of appetite
- When these medications are required, assistance from a Pain Medicine specialist is often helpful

## Other Interventions: Chronic Pain Rehab Program

- Some patients with chronic pain benefit from a multidisciplinary program tailored to their needs
- CPRP integrated services include: pain medicine management designed to minimize opioids, counseling (individual and group), biofeedback, and physical/occupational therapies
- Options include inpatient, day care, or outpatient
- For more information: [clevelandclinic.org/cprp](http://clevelandclinic.org/cprp)

## Other Interventions: Fall Prevention

- Patients with neuropathy are at increased risk of falling
- Suggestions to help reduce patient fall risk:
  - Ask about falls at each office visit
  - Assess of gait and balance at each office visit
  - Prescribe an assistive device if appropriate
  - Refer to physical therapy for gait assessment/retraining
  - Suggest participation in a water exercise program (or other low-impact activity) for strength and balance
  - Arrange a home safety evaluation for hazard modification
  - Manage of other conditions likely to increase the risk of falls (e.g., regular eye examinations and vision correction)