



Managing Neuropathy after Transplant

Celebrating a Second Chance at Life
Survivorship Symposium

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Managing Neuropathy after Transplant

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Objectives

- Definition of peripheral neuropathy
- Causes of neuropathy in transplant population
 - Chemotherapy-induced peripheral neuropathy (CIPN)
 - Graft-versus-host diseases (GVHD)
- Testing for peripheral neuropathy
- Management of peripheral neuropathy

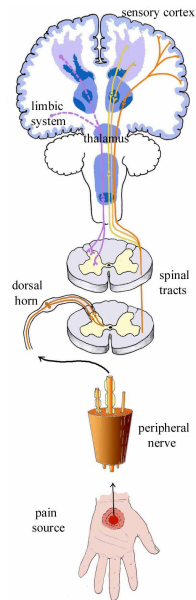


Definition

- Peripheral neuropathy is not a single disease. It's a general term for a series of disorders that result from damage to the body's peripheral nervous system.
- Peripheral neuropathy occurs when nerves are damaged or destroyed and can't send messages from the brain and spinal cord to the muscles, skin and other parts of the body.
- When damage occurs, numbness and pain in these areas may occur.



Simple Pathway of Pain



- Pain receptors found everywhere except the brain
- Pain impulse is sent to dorsal horn of spine
- Basic sensation of pain occurs at the thalamus
- Continues to limbic system (emotional center) and cerebral cortex to be perceived and interpreted

Peripheral Neuropathy

- In the general population 2.4% of people have neuropathy
- The incidence increases to 8% in people older than 55
- Peripheral neuropathy is more common in people with diabetes, HIV and those receiving chemotherapy (CIPN)
- Other causes of peripheral neuropathy
 - Nutritional - B12 deficiency
 - Underlying disease the transplant was for
 - Kidney disease
 - Alcohol
 - Rare immune mediated neuropathy

Risk Factors for Peripheral Neuropathy

- Predisposing risk factors for peripheral neuropathy:
 - patient age, higher risk in older patients
 - the occurrence of neuropathy before the start of chemotherapy
 - a history of smoking
 - impaired renal function with reduced creatinine clearance



Symptoms of Peripheral Neuropathy

- Sensory
 - Tingling/prickling
 - Dead numbness
 - Cold
 - Tightness
 - Burning
 - Shooting/stabbing pains
 - Sensitivity to contact



Symptoms of peripheral neuropathy

- Weakness
 - Feet slapping
 - Trouble arising from a chair or toilet seat
 - Decreased grip strength



Symptoms of Peripheral Neuropathy

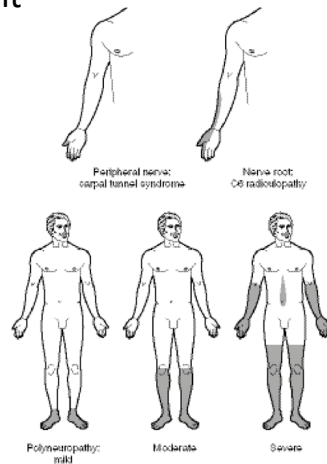
- Autonomic nervous system controls the body functions that we do not consciously think about. As a result of neuropathy, you might experience
 - Lightheadedness upon standing
 - Dry eyes/dry mouth
 - Feeling full after eating a few bites or small meal
 - Constipation/diarrhea
 - Difficulty voiding
 - Lack of sweating
 - Erectile dysfunction



- Peripheral neuropathies of many different causes present with similar symptoms and signs

Stocking glove

- Most common is length-dependent
 - Sensory involvement is most severe



Chemotherapy Induced Peripheral Neuropathy (CIPN)

- The prevalence of CIPN is agent-dependent, with reported rates varying from 19% to more than 85%
- Most common agents are
 - Platinums
 - Taxanes
 - Thalidomide and Lenalidomide
 - Bortezomib (Velcade)
 - Vincristine
 - Brentuximab Vedotin
- Toxicity may occur either with a high single dose or after cumulative exposure.

Graft-versus-Host Disease and Neuropathy

- Neuropathy as a manifestation of GVHD is most commonly seen as chronic graft-versus-host disease.
- Median time between transplant and onset of neuropathy is 6 months
- Neurologic GVHD more often affects the peripheral nervous system
- Higher prevalence of neuropathy in patients with scleroderma
- It is usually associated with long-term immunosuppression and GVHD.



Testing for Peripheral Neuropathy

- Light touch testing using a monofilament



- Vibration testing with a tuning fork



Testing for Peripheral Neuropathy



Pin prick test

- Other testing should include:
 - Test strength – manual muscle examination
 - Test reflexes
 - Evaluate gait (walking)

Treatment Options

- Topicals
 - Patches: lidocaine
 - Anti-inflammatory: Diclofenac
 - Creams: capsaicin
- Oral
 - Currently, duloxetine is the only agent endorsed by the ASCO and ESMO guidelines for treatment for CIPN
 - Gabapentin
 - Lyrica
 - Tri-cyclic antidepressants/psychotropic medications
 - Nutritional supplements/vitamins
- Mechanical
 - Acupuncture, Massage or TENs

First-line Treatments

- Soaking the feet in cool water
 - Epsom salt soaks
- Over-the counter pain medications
- Topical agents
 - Capsaicin
 - Lidocaine patch or gel
 - 5% patch – maximum of 3 patches daily for a maximum of 12 -18 hours, trial for 3 weeks
 - No significant adverse effects
 - Combination gels/creams
 - Amitriptyline 1%/Ketamine 0.5%
 - Also can use Baclofen, Clonidine, Lidocaine



Potential Advantages of Compounded Topical Agents

- Avoids the GI tract
 - Greater concentration of drug is delivered directly to the area where it is applied
 - Not dependent on blood flow for delivery to site
- Lower systemic drug levels
 - ↓ Toxicity
 - ↓ Drug interaction potential
- Improved compliance may be possible
- Multiple ingredients
 - Anti-inflammatory, numbing agents, vitamins, supplements
- Flexible dosing (concentration)



Second-line Treatments

- Oral medications
 - Antidepressants that change the brain chemistry and communication in the brain cell to help relieve pain symptoms.
 - Duloxetine (Cymbalta®)
 - Venlafaxine (Effexor®)
 - Tricyclic antidepressants
 - amitriptyline, nortriptyline or desipramine
 - Anti-Seizure
 - Gabapentin (Neurontin®) and pregabalin (Lyrica®)



Other Medications

- Anti-epileptic medications
 - Carbamazepine, oxcarbazepine, valproic acid
- Pain medications
 - Tramadol
 - Oxycodone, both long acting and immediate release
 - Morphine sulfate, both long acting and immediate release



Medical Marijuana

- Consider for use in refractory neuropathic pain after failing 2-3 prior lines of therapy
 - CBD Oil: highest dose in trials was 30mg per day
 - THC sprays
 - Synthetic THC:
 - Nabilone 1-2mg twice a day
 - Dronabinol 2.5-10mg twice a day
- Side effects: psychosis, euphoria, paranoia, hypotension
- With prolonged use do not stop without taper due to withdrawal symptoms



Nonpharmacologic Treatments

- Cognitive-behavioral therapy
 - Can be self guided or with group therapy
- Neurofeedback
 - involves auditory or visual stimuli or rewards when voluntary changes are made in brain activity within a designated neurofeedback
 - resulted in significantly improved CIPN-related pain, sensory symptoms, quality of life and fatigue.



Mezzanotte, J.N., Grimm, M., Shinde, N.V. *et al.* Updates in the Treatment of Chemotherapy-Induced Peripheral Neuropathy. *Curr. Treat. Options in Oncol.* **23**, 29–42 (2022). <https://doi.org/10.1007/s11864-021-00926-0>

Nonpharmacologic Treatments

- Cryotherapy and compression therapy
 - Cryotherapy involves cooling the skin surface in an attempt to limit the local effects of chemotherapy. This can involve limb-induced hypothermia or cooling gloves or socks
 - It is often combined with compression therapy, a process that utilizes elastic stockings or surgical gloves to apply diffuse pressure to the skin surface.
 - Used for the prevention of CIPN, prophylactic cryotherapy has been shown to reduce the risk of dose reduction of taxane-based chemotherapy.



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Nonpharmacologic Treatments

- Scrambler therapy:
 - involves the use of a device that delivers electrocutaneous stimulation to the skin and is designed to replace endogenous pain signals.
 - Data from randomized controlled trials has been mixed and is less promising. Additional studies in this area are needed.



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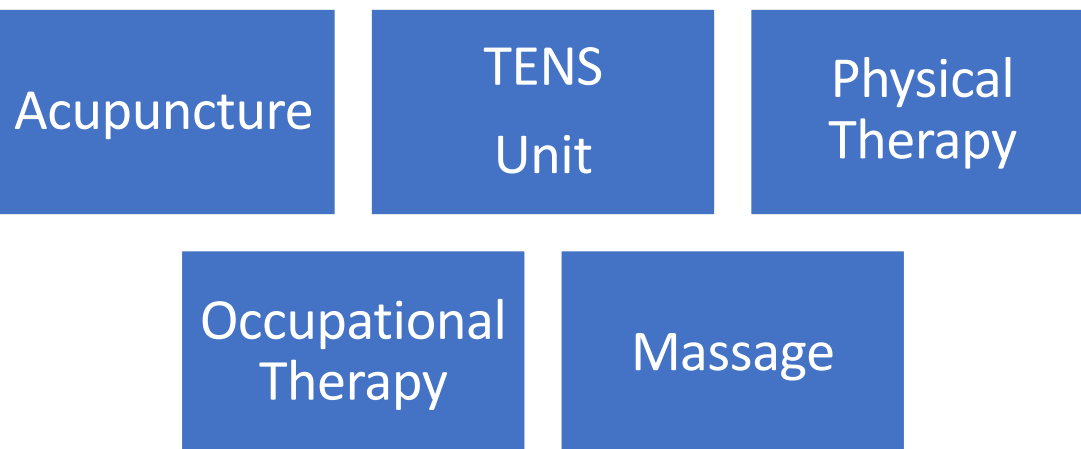
Nonpharmacologic treatments

- **Sensorimotor training and whole-body vibration training**
 - patients in the intervention groups reported subjective improvement of CIPN symptoms and also had objective improvement in tendon reflexes and pain control in the sensorimotor training and whole-body vibration training groups, respectively.



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Mechanical Treatment



General Foot Care

- Any small injury to the skin can result in a serious infection and/or sores
- Report any injuries to your feet to your health care provider right away
- To avoid injuries:
 - Do not cut or file corns, callouses
 - Do not use chemicals on the feet
 - Wear shoes or sturdy slippers at all times
 - Do not apply direct heat to your feet and legs



Daily Foot Care



Daily Foot Care

- Care for nails – cut nails straight across, being careful not to injure surrounding skin
- Do not go barefoot
- Wear clean seamless socks
- Wear shoes or sturdy slippers at all times even at night
- Look inside shoes before putting them on
- Choose good footwear – closed toe, lightweight, low heels, laces or straps



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[Pharmacological Reviews](#) 2021, 101:1–259–201



Questions?



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