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.

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 GHVD 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

- 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
- Epson 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.

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.


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.

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**

- Acupuncture
- TENS Unit
- Physical Therapy
- Occupational Therapy
- Massage
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

- Wash your feet daily with lukewarm water
- Test the temperature with your hands
- Use a mild fragrance-free soap and wash gently
- Apply a skin moisturizer without alcohol or perfume
- Dry by blotting or patting
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

References

- Nanna Brix Finnerup, Rohini Kuner, and Troels Staehelin Jensen; Neuropathic Pain: From Mechanisms to Treatment. Physiological Reviews, 2021 101:1, 269-301

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Questions?

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