



5. Guidelines and Standards

Currently, no guidelines or standards exist for the assessment or management of chemotherapy-induced peripheral neuropathy. The American Society of Clinical Oncology (ASCO) (1999) clinical practice guidelines for the use of chemotherapy and radioprotectants provide evidence related to the prevention of chemotherapy-induced neurotoxicities and can be found at www.asco.org (also see *Pharmacologic Interventions below*).

Peripheral Neuropathy

Monitoring Parameter(s)

- Perform subjective and objective assessment of symptoms related to peripheral neuropathy: pain, numbness, burning, tingling, paresthesias, and ability to perform fine motor skills.
- Perform objective assessment of symptoms related to peripheral neuropathy: deep tendon reflexes, vibration sensation, touch, proprioception, muscle strength, cranial nerve assessment (particularly vision and hearing), orthostatic blood pressure measurement, and Lhermitte's sign.
- Assess for the presence of factors related to peripheral neuropathy: neuropathic pain syndromes and depression.
- Assess for motor neuron-related signs of neuropathy: muscle weakness and atrophy, hypotonia, hyporeflexia, or areflexia.
- Assess for sensory neuron-related signs of neuropathy: burning pain, paresthesias, and dysesthesias, including loss of proprioception, ataxia, loss of balance, and a decrease in vibration sensation.
- Assess for signs of autonomic dysfunction related to peripheral neuropathy: constipation, paralytic ileus, and urinary retention, orthostatic blood pressure alterations, sexual dysfunction.
- Assess for the presence of preexisting neuropathies related to other illnesses or disease states: diabetes, human immunodeficiency virus, alcoholism, and hereditary conditions (e.g., Charcot Marie Tooth Disease).
- Quantitative tests: Quantitative Sensory Testing (QST) nerve conduction studies, electromyograms and sural nerve biopsy may be performed for diagnostic purposes or as correlates to clinical symptoms. Little data supports the routine use of quantitative testing to make a confirmatory diagnosis of chemotherapy-induced peripheral neuropathy because the diagnosis is typically made by clinical presentation. The use of QST in determining the presence of diabetic neuropathy is increasing, as it provides information concerning large and small peripheral nerve fibers. The use of QST has been tested in few studies of chemotherapy-induced neuropathy.

Intervention (s)

- *Exercise Therapy*
 - Few studies address the value of exercise for individuals with peripheral neuropathy.
 - Performing passive range of motion exercises enhances reinnervation in denervated muscle and appears to have therapeutic value.
 - Some evidence suggests that resistance exercises may be of benefit in increasing strength for individuals weakened by neuropathy.
 - Refer clients to a physical therapist for orthotic braces or a splint to assist with lower-extremity alignment and balance.
 - Exercise therapy must take into consideration safety issues in regard to peripheral neuropathy. Loss of sensation and muscle weakness in the lower extremities limit patients' abilities to sense changes in terrain, predisposing them to falls.

- *Occupational Therapy*
 - The individual with an occupation requiring fast-paced mobility may require vocational counseling.
 - Assesses clients' capabilities to perform self-care activities and recommend assistive devices as needed.

- *Educational Interventions*
 - Teach clients strategies for managing personal safety, such as using visual input to compensate for loss of lower-extremity sensation in navigating changing terrain.
 - Teach clients about the risk for ischemic or thermal injury resulting from loss of sensation in extremities.
 - Teach strategies for symptoms of autonomic dysfunction (postural hypotension, constipation, urinary retention), such as dangling the legs prior to arising and the use of a high-fiber diet, adequate fluid intake, and exercise.

- *Pharmacologic Interventions*
 - *Cytoprotective agents*, such as amifostine (Ethyol[®], ALZA Corporation, Mountain View, CA) has shown some efficacy in reducing the incidence and severity of the neurotoxicity experienced. However, at this time, ASCO's Clinical Practice Guidelines (1999) concluded that insufficient data support the routine use of amifostine to prevent cisplatin or paclitaxel-induced neuropathy.
 - *Calcium and magnesium infusions* may hold promise in the prevention of oxaliplatin -induced neurotoxicity. One study by Gamelin et al. (2004) has investigated the use of calcium gluconate

and magnesium chloride infusions as a preventative approach to oxaliplatin-induced neurotoxicity. Not enough evidence supports the routine use of calcium and magnesium infusions in the prevention of neuropathy. Currently, a prospective randomized multicenter, double blind, placebo controlled trial is underway to investigate this further (Gamelin et al., 2004).

- o *Glutamine*, an amino acid, has been proposed as a neuroprotective agent and as a mediator in the myalgia and arthralgias that accompany cisplatin, paclitaxel and vincristine therapy. Studies indicate that glutamine may offer a reduction in severity of neuropathy, especially with dose-intensive paclitaxel therapy. The manner in which glutamate offers neuroprotection is not yet known, and further trials are in progress.
- o *Glutathione* is a natural thiol tripeptide involved in protective mechanisms resulting from oxidative injury, and in the prevention of platinum accumulation in the dorsal root ganglia. Studies of using glutathione in the prevention of cisplatin-induced neuropathy have been inconsistent, and further studies are needed.
- o *Neurotrophic factors*, such as recombinant nerve growth factor (rhNGF), are currently in phase II and III clinical trials. Preliminary reports suggest that they have variable success, and more data will be needed before recommendations about use can be made.
- o *Pain control measures: Tramadol hydrochlorid* (Ultram[®], Ortho-McNeil Pharmaceutical, Inc., Raritan, NJ), *tricyclic antidepressants*, and *gabapentin* (Neurontin[®], Pfizer Inc., New York, NY) have shown some degree of efficacy in the management of neuropathic pain. Additional trials are needed to confirm efficacy.
- o *Other agents*, such as ORG 2766 (a corticotropin analog), venlafaxine (Effexor[®], Wyeth Pharmaceuticals Inc., Madison, NJ), and acetyl-L carnitine also are being studied for their effectiveness in the prevention of chemotherapy-induced peripheral neuropathy, and trials are still in progress.

Comments. Depression can accompany neuropathic pain syndromes. Antidepressant agents can enhance the action of pain medication regimens in these cases.