Chemotherapy-Induced Peripheral Neuropathy

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This article has been chosen as being particularly suitable for reading and discussion in a Journal Club format. The following questions are posed to stimulate thoughtful critique and exchange of opinions, possibly leading to changes on your unit. Formulate your answers as you read the article.

1. Is this article research based? Can we assess the level of evidence being presented?
2. How often do we care for patients at risk for peripheral neuropathies?
3. Describe a situation in which a patient has experienced these side effects. How were the symptoms discerned? What were the patient's complaints? How did occurrence of the symptoms affect the course of the chemotherapy?
4. What assessment parameters do we use to identify patients at risk for or experiencing peripheral neuropathies?
5. How can we improve patient education regarding peripheral neuropathies?
6. What nondrug interventions can we use to treat these symptoms?

At the end of the session, take time to recap the discussion and make plans to follow through with suggested strategies.

Purpose/Objectives: To review the literature documenting the scope, treatment, and prevention of chemotherapy-induced neuropathy.

Data Sources: Published abstracts, primary research literature, and textbook chapters.

Data Synthesis: Recent improvements in the management of other treatment-related toxicities have led to peripheral neuropathy becoming a dose-limiting toxicity of commonly used chemotherapeutic groups such as platinols, vinca alkaloids, and taxanes.

Conclusions: The nervous system has not been the focus of education or training for oncology nurses. Therefore, nurses' ability to educate patients regarding this aspect of their condition has been limited.

Implications for Nursing: With its significant impact on quality of life, peripheral neuropathy treatment and prevention are important components in the care of patients with cancer.

In 1987, Holden and Felde noted that "much of the difficulty educating individuals about peripheral neuropathy arises as a result of lack of knowledge on the parts of physicians and nurses " (p. 13). This still is true today. The nervous system has not been the focus of education or training for oncology nurses. As a consequence, their comfort and ability to educate patients have been limited. Recent improvements in the management of other treatment-related toxicities have led to peripheral neuropathy becoming a dose-limiting toxicity of three commonly used chemotherapeutic groups, particularly platinols, vinca alkaloids, and taxanes. This recognition has made peripheral neuropathy an important component in the care of patients with cancer.

Key Points . . .

- The peripheral nervous system is comprised of three functional divisions: autonomic, motor, and sensory.
- Peripheral neuropathy is a dose-limiting toxicity of cisplatin, paclitaxel, and vincristine and commonly is associated with oxaliplatin and bortezomib.
- Baseline and continued assessment are imperative for early diagnosis.
- Anticonvulsants and antidepressants are the mainstay of treatment for neuropathic pain.

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Pathophysiology

The peripheral nervous system is comprised of three functional divisions: the sensory nerves, which sense touch, pain, temperature, position, and vibration sense; the motor nerves, which are responsible for voluntary movement, muscle tone, and coordination; and the autonomic nerves, which control intestinal motility, blood pressure, and involuntary muscles. Peripheral neuropathy is defined as any injury, inflammation, or degeneration of the peripheral nerve fibers (Almadrones, Armstrong, Gilbert, & Schwartz, 2002). Anatomically, two types of peripheral nerve fibers exist. Small fiber nerves are unmyelinated and include nerves that sense pain and temperature. Large fiber nerves are myelinated and sense position and vibration along with motor control. Small fiber nerves are composed primarily of microtubules, which act as the transport mechanism for proteins. Large fiber nerves are composed primarily of neurofilaments, which serve as the framework of the axon. These sensory fibers terminate at the level of the skin and muscle. The axon then extends caudally to the dorsal root ganglion, where the cell body is located. It then connects with the either dorsal column (large fiber) or spinothalamic tract (small fiber) in the spinal cord (see Figure 1). These tracts then act as a relay station to the sensory areas of the brain.

Peripheral neuropathy is associated with numerous conditions in the general population (e.g., diabetes, vitamin deficiencies) but generally is classified as hereditary or acquired. In an article by Dyck, Dyck, Grant, and Fealey (1996), 26% of patients presenting with peripheral neuropathy had no discernable cause. Certain disease states, such as vitamin B_{12} deficiency, diabetes, hypothyroidism, and paraneoplastic diseases, can be associated with peripheral neuropathy. Table 1 provides a summary of the type of neuropathy associated with each of these conditions and symptoms.

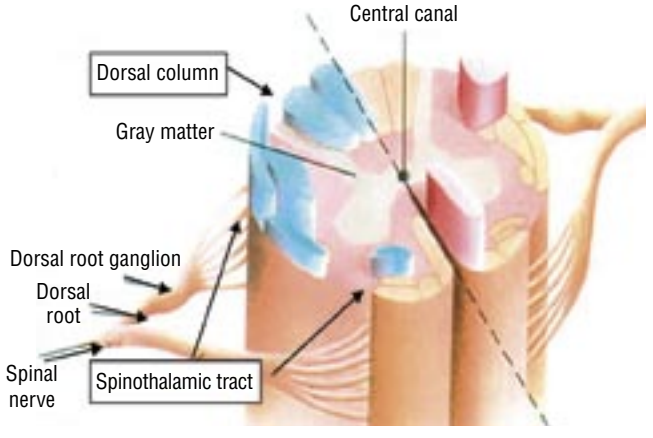
Peripheral neuropathy is estimated to occur in 10%–20% of patients with cancer. In a series of studies of patients with lung cancer performed by Teravainen and Larsen (1977), 48% had clinically evident peripheral neuropathy, most of them prior to receiving chemotherapy. The severity of neuropathy in patients with cancer ranges from mild distal paresthesias to symptoms severe enough to render a person bed ridden and unable to ambulate. The overall incidence of chemotherapy-related peripheral neuropathy is not known, but the condition is associated with several chemotherapeutic agents. Table 2 provides an overview of such agents and types of neuropathy. The incidence and severity of neuropathy associated with certain agents are such that the condition now is recognized as a dose-limiting toxicity, warranting more extensive discussion. The agents are paclitaxel, cisplatin, vincristine, oxaliplatin, and bortezomib.

For an agent to cause peripheral neuropathy, it first must be able to cross the blood-nerve barrier, and the nervous system must be sensitive to the agent. In addition, predisposing conditions mentioned earlier or the use of other agents known to cause neuropathy also may affect its occurrence. In most cases, peripheral neuropathy is related temporally to administration of a drug (i.e., the neuropathy occurs within hours, days, or weeks of drug delivery). The exception is cisplatin, which is known to cause a delayed neuropathy that may become symptomatic several months after the drug has been given. Chemotherapy-induced peripheral neuropathy presents in a stocking-glove distribution, where the point most distal from the trunk is affected first (e.g., fingertips and toes), and then it progresses medially toward the trunk. Lastly, most agents tend to affect one fiber more than another (e.g., cisplatin affects large fibers, paclitaxel and vincristine affect small fibers). All of the agents that cause peripheral neuropathy can lead to loss of deep tendon reflexes.

Table 1. Differential Diagnosis of Peripheral Neuropathy in Patients With Cancer

Cause	Neurotoxic Effect
Vitamin B_{12} deficiency	Large fiber injury
Cachexia	Diffuse weakness
Chemotherapy	Small and/or large fiber injury
Charcot-Marie-Tooth disease	Large fiber injury
Diabetes	Small fiber injury
Atherosclerotic ischemic disease	Sensory neuropathy in lower extremities
Paraneoplastic syndrome	Distal sensory or sensorimotor deficit
Thyroid dysfunction	Proximal and distal weakness; carpal tunnel syndrome
Alcoholic neuropathy	Numbness, paresthesias

Note. Based on information from Almadrones et al., 2002.



Cross-section of the spinal cord with sensory tracts labeled

Figure 1. Gross Anatomy of the Spinal Cord With Ascending Tracts Labeled

Note. From *Understanding the Human Body* (p. 128), by P. Tate, R.R. Seeley, and T.D. Stephens, 1994, St. Louis, MO: Mosby. Copyright 1994 by Elsevier, Inc. Adapted with permission.

Chemotherapeutic Agents That Induce Peripheral Neuropathy

Platinum Compounds

Cisplatin: Peripheral neuropathy has been reported to occur in 57%–92% of patients treated with cisplatin (Cersosimo, 1989; Roelofs, Hrushesky, Rogin, & Rosenberg, 1984). The actual pathogenesis of cisplatin-induced neuropathy is unknown (Gilbert, 2000). Neuropathologic studies have found aggregation of neurofilaments found in large fibers, axonal swelling, and loss (Thompson, Davis, Kornfeld, Hilgers, & Standefer, 1984). Therefore, large fibers are affected more severely. The

Table 2. Chemotherapeutic Agents and Neuropathies

Agent	Neuropathy Induced
Cytosine arabinoside	Rare: symmetric sensorimotor polyneuropathy
Interferons	Transient paresthesias
Matulane	Sensorimotor polyneuropathy
Metronidazole	Sensorimotor polyneuropathy
Platinum analogs	Primarily large fiber neuropathy
Vinca alkaloids	Primarily small fiber neuropathy
Taxanes	Mixed sensorimotor polyneuropathy
Thalidomide	Small fiber neuropathy

sensory effect is characterized by loss of the senses of position and vibration. It can be associated with Lhermittes sign (or a lightening-like sensation) that starts in the neck and extends down the back and legs and occurs when a person flexes the neck. It is thought to occur as a result of irritation to the dorsal column in the spinal cord (Cersosimo). Motor dysfunction usually occurs after moderate to marked sensory loss (Furlong, 1993). Autonomic dysfunction is rare but may include orthostatic hypotension.

The occurrence of neuropathy is dependent on the type of platinum analog, total daily dose, and total regimen dose (Almadrones et al., 2002). Cisplatin-induced peripheral neuropathy is reported to occur once the cumulative dose exceeds 300 mg/m^2, although it may be seen at lower doses if prolonged infusions are given (Cavaletti et al., 1992; Pollera, Pietrangeli, & Giannarelli, 1991; Walsh, Clark, Parhad, & Green, 1982). The effect may be severe if the cumulative dose exceeds 500 mg/m^2. Peripheral neuropathy tends to occur late into the treatment course or after therapy has been completed. Von Schlippe, Fowler, and Harland (2001) found that 12% of their patients had symptoms of peripheral neuropathy at the end of bleomycin, etoposide, and cisplatin chemotherapy for testicular cancer and 54% had it three months after the chemotherapy was completed. Most studies have indicated that 66% of patients will have full recovery, with some patients taking two years for this to occur.

Oxaliplatin: Oxaliplatin is a novel platinum compound that also is associated with peripheral neuropathy. Neuropathy is thought to be related to oxaliplatin's ability to interfere with axonal ion conductance, altering neuronal excitability. Two types of neuropathy have been reported. The first is similar to that seen with cisplatin: a distal sensory neuropathy involving primarily large fibers. Quasthoff and Hartung (2002) reported that 80% of patients treated with oxaliplatin developed neuropathy, with 40% of them having complete resolution of symptoms in six to eight months. The second type of neuropathy is acute, occurring 30–60 minutes after infusion. Patients often develop dysesthesias of the hands and feet, jaw tightness, and a sensation of a loss of breathing without respiratory distress (pharyngo-laryngo-dysesthesia). Symptoms associated with acute neuropathy have been reported to be aggravated by exposure to cold and are influenced by infusion time and dose. However, most patients experience the symptoms at doses above 540 mg/m^2.

Taxanes

The use of taxanes, particularly paclitaxel (Taxol®, Bristol-Myers Squibb Company, New York, NY), has brought the issue of peripheral neuropathy to the forefront of cancer symptom management. The risk for individual patients is dependent on the agent used, administration schedule, cumulative dose, and potentially whether it is combined with other neurotoxic agents (Almadrones et al., 2002). Paclitaxel is reported to cause peripheral neuropathy in 60% of all treated patients (Bristol-Myers Squibb Company, 2000). Taxanes are plant-derived poisons of the mitotic spindle apparatus and cause microtubular aggregation (Pazdur, Kudelka, Kavanagh, Cohen, & Raber, 1993). Paclitaxel produces a mild to moderate sensorimotor neuropathy in most patients receiving doses of at least 200 mg/m^2, which generally remains mild until cumulative doses exceed 1,400 mg/m^2 (Rowinsky, Chaudhry, et al., 1993; Rowinsky, Eisenhauer, Chaudhry, Arbuck, & Donehower, 1993; van Gerven et al., 1994). The incidence of all grades of neuropathy with docetaxel (Taxotere®, Sanofi-Aventis, Bridgewater, NJ) is reported to be 49% (Aventis Pharmaceuticals, 2003). Neuropathy associated with docetaxel tends to be dose-dependent and usually is not recognized until the cumulative dose exceeds 600 mg/m^2 (Hilkens et al., 1996). Small fibers are affected most, although axonal injury and focal areas of demyelinization also occur in large fibers (Lipton et al., 1989). Neuropathy can develop in one to three days after treatment, and continued therapy leads to progressive neurologic dysfunction (Lipton et al.). Patient-reported quality-of-life evaluations of those receiving taxanes were significantly negatively associated with patient neuropathy scores. As neuropathy increased, quality of life decreased (Hay, 2002).

Recent trials have compared the toxicities of paclitaxel-carboplatin with docetaxel-carboplatin. Vasey (2002) reported a statistically lower incidence of arthralgic/myalgic symptoms, a lower overall incidence of sensory and motor neurotoxicity, and withdrawal of therapy as a result of neurotoxicity during treatment with docetaxel. Another trial found a low incidence of neurotoxicity in patients with ovarian cancer receiving docetaxel-carboplatin (Rapoport et al., 2002).

Vinca Alkaloids

Peripheral neuropathy has been reported with vincristine, vindesine, and vinblastine, but neurotoxic potential is greatest with vincristine (Kaplan & Wiernik, 1982). The risk of neuropathy is related to the type of vinca alkaloid and dose (Almadrones et al., 2002; Hohneker, 1994). Neuropathy usually is seen when the cumulative dose of vincristine received exceeds 6 mg/m^2 or a cumulative dose of 15–20 mg, and individual doses of greater than 2 mg are less well tolerated (Legha, 1986; Roca et al., 1985). Paresthesias in the hands or feet are reported to occur in as many as 57% of patients receiving vincristine therapy, with motor weakness or foot drop occurring in 22%–34% (Furlong, 1993). Vincristine also is known to cause peripheral neuropathy by causing aggregation of microtubules (the framework of the axon), leading to degeneration and atrophy of the peripheral nerve fibers. It affects small and large fibers, usually causing a stronger effect on small fibers. Presenting symptoms are loss of pain and temperature sensation. The earliest symptoms are myalgias, distal paresthesias, and a decrease in ankle jerks (Rosenthal & Kaufman, 1974). In addition, jaw pain and other muscle cramps can occur shortly after administration (Haim, Barron, & Robinson, 1991).

Autonomic effects of vinca alkaloids can include intestinal dysmotility and orthostatic hypotension. In addition, impotence, urinary retention, and abnormal cardiovascular reflexes, manifested as abnormal pulse responses, have been reported (Roca et al., 1985). Motor symptoms also may be associated with sensory deficits. The most common motor symptom is foot drop, or weakness of dorsiflexion of the ankle. Cranial nerve effects are rare but may include jaw pain, vocal cord palsy, or extraocular palsy (Holland et al., 1973). Peripheral neuropathy has been reported to occur immediately after administration of vinca alkaloids or several weeks after. Recovery of sensation and reflexes has been reported to occur in 66% of those treated.

Proteasome Inhibitors

Bortezomib: Bortezomib is a novel dipeptide boronic acid small molecule that has shown antitumor activity in patients with multiple myeloma and is undergoing investigation in other hematologic malignancies and solid tumors (Richardson, 2003). Several studies have shown peripheral sensory neuropathy that may be dose-limiting associated with dosages greater than 1.6 mg/m^2. Patients often presented with an atypical neuropathic pain syndrome that became a more recognized stocking-glove distribution. Most of the patients who experienced neuropathy had been pretreated heavily with known neurotoxic agents, and several had a baseline grade I neuropathy on entry into study (Aghajanian et al., 2002). Aghajanian et al. suggested careful monitoring of patients started on treatment with bortezomib, especially those who may have been exposed to other neurotoxic agents.

Assessment

The importance of baseline neurologic assessment cannot be overemphasized. It affords nurses the ability to recognize comorbidities that may place patients at greater risk of developing neuropathy or preexisting neuropathy prior to initiating chemotherapy treatment. It alerts healthcare teams and patients to the risk of neuropathy and may alter treatment plans.

A comprehensive assessment of motor, sensory, and autonomic function before, during, and after chemotherapy treatment is necessary to evaluate history and causes of neurotoxicities. With the exception of delayed cisplatin-induced neurotoxicity, most signs and symptoms of peripheral neuropathy that occur during and soon after chemotherapy administration suggest drug-induced neurotoxicity. Table 3 outlines components included in the evaluation of patients suspected of being at risk for chemotherapy-induced peripheral neuropathy. The components of assessment include history, gait, reflexes, strength, and autonomic and large and small fiber senses. Patients should be observed walking into the room. Abnormalities of gait, such as shuffling or high stepping, can be assessed, as well as evidence of pain with walking. To assess the motor system, comparisons of distal to proximal muscle strength should be assessed in the upper and lower extremities. Patients experiencing weakness from peripheral neuropathy will have bilateral distal weakness first. Components of the sensory assessment also should compare the ability to sense distally as compared to proximally. Patients receiving agents known to affect small fibers more readily (e.g., vinca alkaloids, taxanes) should have their pain assessed. Patients receiving agents known to affect large fibers more readily (e.g., cisplatin) should have their sense of vibration and proprioception assessed. The final component of assessment should be autonomic function. This is especially important in those receiving vinca alkaloids.

Table 3. Screening Assessment for Peripheral Neuropathy

Type of Function	Assessment
Gait	Observe patient ambulating. Assess for wide-based gait, steppage gait, or signs of pain when ambulating.
Motor	Assess for distal versus proximal weakness and symmetry. Lower extremity: foot dorsiflexion versus hip flexor strength Upper extremity: interosseous or hand grasp strength versus deltoid strength
Reflexes	Lower extremity: Achilles and patellar reflexes Upper extremity: brachioradialis and biceps reflex
Sensory	Assess for distal loss and proximal progression. Large fiber: position and vibration sense in great toe to ankle and knee and finger to wrist and elbow Small fiber: pinprick sensation from great toe up each leg to point where normal sensation and from finger up arm to point where normal sensation
Autonomic	Assess bowel sounds, orthostatic blood pressure, and pulse variation with Valsalva maneuver.

Simply asking patients about the existence of neuropathy may be as important as sophisticated testing. Rambaud et al. (2001) found that rigorous clinical history-taking was as sensitive as somesthetic evoked potentials (i.e., quantified sensory testing) in discriminating clinically relevant neuropathy in patients receiving oxaliplatin.

Prevention

No treatment is available to reverse neuropathy, but some steps can be taken to prevent or reduce its occurrence. The first is to recognize and treat any preexisting conditions (e.g., B_{12} deficiency, diabetes). The issue of toxic synergy also should be addressed. For example, does the patient have a peripheral neuropathy related to diabetes, and is he or she scheduled to receive an agent known to cause a similar neuropathy? May another treatment option be as effective with fewer side effects? All patients should be monitored carefully during therapy, with frequent assessments specific to the occurrence of peripheral neuropathy since the last treatment. Once neuropathy occurs, continuing the same therapy may lead to progressive nerve damage and loss of function.

Some researchers have interest in the use of cytoprotective agents to reduce neuropathy associated with cancer. Cavaletti and Zanna (2002) provided an excellent overview of agents that currently are used, as well as agents currently undergoing clinical investigation. Two agents have shown promise in reducing the incidence of peripheral neuropathy. Amifostine, approved for the prevention of renal toxicity associated with cisplatin, has had mixed results reducing neuropathy. Although the exact mechanism of action is not known, studies completed on animal models have shown sparing of nerve fibers and protection of the amplitude and area of the compound muscle action potential in eletroneurography studies (Yalcin et al., 2003). Lorusso et al. (2003) reported a

statistically significant decrease in the overall incidence of neuropathy associated with paclitaxel and carboplatin, but Cavaletti and Zanna found no benefit. Results from studies with single-agent paclitaxel and vincristine have not been positive (Kaplan et al., 2001; Kemp et al., 1996).

Glutamine, a naturally occurring amino acid, has shown benefit in reducing peripheral neuropathy associated with paclitaxel. Researchers have theorized that glutamine serves as a neuroprotectant by upregulating nerve growth factor, which in animal models has been shown to be decreased when peripheral neuropathy occurs (Vahdat et al., 2001). Vahdat et al. evaluated peripheral neuropathy in a small number of patients receiving high-dose paclitaxel 825 mg/m^2. Patients were given glutamine 10 g three times a day starting 24 hours after administration of paclitaxel and continuing for four days. Statistically significant differences were found in reported dysesthesias, motor symptoms, deterioration of gait, and difficulty with activities of daily living in the patients treated with glutamine. However, another study found no benefit over placebo when giving glutamine for preventing paclitaxel-associated myalgias and arthralgias (Jacobson et al., 2002).

Treatment

Pain Management

Neuropathic pain can occur as a result of chemotherapy-induced peripheral neuropathy. The exact pathophysiologic mechanism causing the pain is not known, but it has been theorized to arise from the injured nerve fibers or intact fibers located in the same vicinity (Schaible & Richter, 2004). Ectopic discharges occur in the A-delta and C fibers in the skin, leading to the release of neuropeptides such as substance P. Mechanisms that produce these discharges include changes in the expression of ionic channels, pathologic activation of axons by inflammatory mediators, and pathologic activation of injured nerve fibers by the sympathetic nervous system (Schaible & Richter). The signals then travel through the dorsal horn of the spinal cord. In the spinal cord, the pathologic nociceptive signals lead to central sensitization, which amplifies the processing of the nociceptive input. Neuropathic pain often can be characterized by "wind up" or escalation of the pain, even when the offending agent has been removed. Various neuropeptides, such as substance P and neurokinin A, as well as neurotransmitters such as glutamate, facilitate this sensitization. Further discussion of the mechanisms associated with pathologic neuropathic pain are complex and beyond the scope of this article. Schaible and Richter provided an excellent overview. Several terms that are important to understand when describing neuropathic pain are described in Table 4.

The mainstay of pharmacologic treatment is the use of antidepressants and anticonvulsants. Other agents, such as topical analgesics and opioids, also may be effective. Table 5 provides a list of agents that have been used to treat neuropathic pain associated with conditions such as diabetes. The agents have been used to treat patients with neuropathic pain related to chemotherapy based on the response in other disease states associated with neuropathy, such as diabetes.

Table 4. Terms Used to Describe Neuropathic Pain

Term	Definition
Allodynia	Evoked pain from a stimulus that usually does not cause pain
Dysesthesia	An unpleasant abnormal sensation
Paresthesia	Sensation of numbness, prickling, or tingling
Anesthesia	Lacking sensation

Nondrug Interventions

A plethora of nondrug therapies have been proposed for use in the treatment and prevention of neuropathic pain, from physical therapy, massage, and electrical stimulation to the use

Table 5. Pharmacologic Interventions for Peripheral Neuropathy Pain

Class and Drug	Usual Starting Dose (mg Per Day)	Usual Effective Dose (mg)
Alpha-2-adrenergic agonist		
Clonidine	–	–
Anticonvulsants		
Carbamazepine	200	600–1,200
Phenytoin	300	Dosed to effectiveness
Valproic acid	10–15 per kg per day in 1–3 doses	750–2,000
Gabapentin	300	300–3,600
Antidepressants: tricyclics		
Amitriptyline	10–25	50–150
Clomipramine	10–25	50–150
Desipramine	10–25	50–150
Doxepin	10–25	50–150
Imipramine	10–25	50–150
Nortriptyline	10–25	50–150
Antidepressants: selective serotonin reuptake inhibitors		
Fluoxetine	10–20	20–40
Paroxetine	20	20–40
Sertraline	50	150–200
Citalopram	20	–
Corticosteroids		
Dexamethasone	Initial: 10	–
Prednisone	Chronic: 1–2	
Local anesthetics		
Mexiletine	150	900–1,200
Tocainide	400	1,200–1,600
Lidocaine	Brief infusion: 2–5 per kg over 20–30 minutes	
	Continuous infusion: 2.5 per kg per hour	Same
	Transdermal 5% patch	Up to three patches
Opioids		
Morphine Hydromorphone Oxycodone Fentanyl Methadone	Dose determined by patient tolerance	Dose titrated to analgesia

Note. Based on information from Almadrones et al., 2002

of complementary and alternative treatments such as vitamin therapy, which has not been studied well (see Figure 2). Patients often pursue alternative therapies independently from health-care providers and sometimes without informing them.

Some patients may derive benefit from complementary and alternative interventions simply because they feel the need to do something, whereas others may derive benefit from a placebo effect. Neutraceuticals and other poorly regulated dietary supplements have the potential to interact with other drugs patients may be taking or have unexpected adverse effects. Such substances also are not reimbursed by most insurance plans. Acupuncture has been studied for years, but little data exist on its use in neuropathies. Patients often turn to therapeutic magnets, which have been shown to have no biologic effect but are harmless (if expensive) (Barbano, Hart-Gouleau, Pennella-Vaughan, & Dworkin, 2003).

Exercise may produce general benefits, including improved quality of life, endurance, circulation, and sensory integration, that can have positive effects on patients with neuropathic syndromes. Physical therapy can aid in the maintenance of muscle strength, function, and prevention of deformities, such as flexion contractures. Physical therapists also can administer transcutaneous electric nerve stimulation, which may increase endorphin release and block noxious sensory impulses through distraction (Barbano et al., 2003).

Hydrotherapy generally is enjoyable for patients, who find enhanced mobility and buoyancy in the water. Resistance exercises can be performed in swimming pools, whirlpools, or Hubbard tanks. Watsu (Chinese aquatic yoga) is relaxing and may improve feelings of well-being. Proper control of water temperature may ameliorate symptoms of heat or cold intolerance. Some patients may have decreased temperature sensation; for such patients, strict avoidance of extremes of heat is essential to avoid injury.

Conventional
- Exercise
- Physical therapy
- Massage
- Transcutaneous electric nerve stimulation

Unconventional (possibly helpful)
- Magnesium replacement
- Distraction therapy
- Humor therapy
- Acupuncture

Unconventional (probably not helpful)
- Magnet therapy (placebo)
- Dietary modification

Figure 2. Nondrug Interventions for Peripheral Neuropathy

- Assess water temperature in the home.
- Use protective gloves while washing dishes.
- Use pot holders.
- Wear cotton socks.
- Keep rooms well lit.
- Clear walkways.
- Use nonskid mats in showers and bathtubs.
- Use soap dispensers instead of bar soap.

Figure 3. Practical Tips to Help Patients With Peripheral Neuropathy at Home

Massage techniques vary from light touch in Swedish massage to deep pressure in shiatsu. Massage is believed to increase circulation, promote relaxation and well-being, and relieve stiffness. However, patients with allodynia or hyperalgesia may not be able to tolerate massage of any sort. One study showed a significant reduction in pain after massage therapy in patients with cancer; therefore, it may be beneficial to reduce neuropathic pain (Cassileth, Vickers, Seidler, & Miner, 2002).

Hypomagnesemia is believed to be associated with an increased risk of neuropathy, and magnesium wasting is an adverse effect of cisplatin therapy (Cersosimo, 1989). However, no data support the notion that magnesium replacement prevents or treats neuropathy. Until conclusive data are obtained, recommending a multivitamin with minerals and magnesium probably is harmless and may provide some benefit.

Knowledge is power, and patients feel empowered when they understand their own disease states. Simple and practical tips can be given to patients to help them at home (see Figure 3). Written information that informs about peripheral neuropathy and safety is available (Almadrones & Arcot, 1999). Also, an excellent resource for patients with neuropathies can be found on the Internet at www.neuropathy.org.

Conclusions

Chemotherapy-induced peripheral neuropathy is a significant, dose-limiting toxicity that affects the lives of patients with cancer. Despite this, limited studies have explored the incidence and course of peripheral neuropathy in this patient population. Studies suggest that improved management of neuropathic pain and interventions to improve functional status have not been achieved. An interdisciplinary approach to this problem, including researchers from various disciplines such as nursing, medicine, physical and occupational therapy, and pharmacology, is needed to address this toxicity as a whole.

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