Chemotherapy-Induced Peripheral Neuropathy: An Algorithm to Guide Nursing Management

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Chemotherapy-induced peripheral neuropathy (CIPN) is a common side effect of many frequently prescribed chemotherapy and biotherapy drugs including taxanes, platinum-based drugs, vinca alkaloids, thalidomide, bortezomib, and interferon. CIPN results in diverse symptom patterns and can lead to physical distress from neuropathic pain, as well as emotional distress, a decrease in functional ability, and social role impairment (Bakitas, 2007; Tofthagen, 2010). Preexisting conditions may predispose patients to develop neuropathy, including diabetes, alcoholism, amyloidosis, HIV, peripheral vascular disease, or nutritional deficiencies (Smith, Beck, & Cohen, 2008; Stillman & Cata, 2006). Symptoms of CIPN may present as exaggerated sensation (neuropathic pain), loss of sensation (numbness, muscle weakness, loss of balance), or both. Symptoms usually present bilaterally and occur in a distal to proximal pattern, beginning in the tips of the fingertips and toes and involving more of the upper and/or lower extremities as CIPN progresses (Visovsky, 2003). Although neuropathic pain causes distress and interferes with physical and emotional function, numbness, muscle weakness, and loss of balance can be more debilitating and may be difficult to quantify using common clinical assessment techniques or gross grading scales.

Oncology nurses play a critical role in the assessment and management of chemotheraphy-induced peripheral neuropathy (CIPN). Baseline and ongoing evaluation of physical function is a critical but often overlooked aspect of assessment of CIPN. The diversity of symptoms and the complexity associated with neuromuscular assessment lead to challenges in evaluation and management of CIPN. To meet this challenge, the authors devised a feasible algorithm to guide oncology nurses in the assessment and management of CIPN using techniques that can easily be implemented in a variety of clinical settings. Managing pain, maintaining safety, and maximizing physical function are the primary goals for nursing management of CIPN.

Oncology nurses play a critical role in assessment and management of CIPN. Research has demonstrated that although nurses recognize the importance of assessing for CIPN, many lack confidence in their assessment skills (Binner, Ross, & Browner, 2011). Neurologic examinations including vibratory testing and reflexes are skills that may or may not guide nurses in recommending interventions for neuropathy because of variation in skill levels and the subjective nature of grading clinical assessments. Baseline and ongoing evaluation of physical function is a critical but often overlooked aspect of assessment of CIPN. The diversity of symptoms and the complexity associated with neuromuscular assessment lead to challenges in evaluation and management of CIPN. To meet this challenge, the authors devised a feasible algorithm to guide oncology nurses in the assessment and management of CIPN using techniques that can easily be implemented in a variety of clinical settings (see Figure 1). The algorithm was developed based on the current literature and the combined clinical expertise of the authors.

In addition to the nursing interventions discussed here, ongoing communication with the oncologist and other members of the healthcare team also is an important aspect of caring for these patients. The guidelines presented in this article are not
meant as a substitute for evaluation and treatment by a neurologist. Instead, suggestions regarding assessment parameters should be communicated to the medical team, and information that will assist the nurse in the determination of appropriate treatments that may prove beneficial to patients is provided.

Initial Screening

Numbness and/or tingling in the distal extremities are considered the hallmark of CIPN and are consistently reported by patients with neuropathy (Tofthagen, 2010). Patients often are hesitant to report neuropathy for a variety of reasons, including fear of discontinuation of potentially life-saving chemotherapy, not wanting to “burden” the clinician, and the perception, which can be perpetuated by clinicians, that peripheral neuropathy is a normal side effect of chemotherapy that must be endured and cannot be adequately treated (Tofthagen, 2010). In addition, although neuropathic pain can be a component of peripheral neuropathy, in many cases either pain is not a factor or patients do not use the expected pain terminology to describe their experience and, therefore, may deny pain when asked. For those reasons, clinicians must be proactive in assessing for signs and symptoms of peripheral neuropathy. A quick and effective way to screen for peripheral neuropathy is to ask every patient receiving chemotherapy, at every visit, whether they have new numbness, tingling, or discomfort in the upper or lower extremities. If they deny any of these symptoms, no additional assessment is needed. If numbness, tingling, or discomfort is affirmed, the next step is to ask a series of three questions regarding (a) neuropathic pain, (b) upper extremity loss of sensation, and (c) lower extremity loss of sensation. The responses to those three questions will determine what additional assessment is needed.

Neuropathic Pain

Neuropathic pain can be defined as “pain arising as a direct consequence of a lesion or disease affecting the somatosensory system” (Dworkin et al., 2010, p. S3). Diagnosing and managing cancer-related neuropathic pain is challenging and often results in inadequate pain management (Smith et al., 2011). Neuropathic pain often is described as burning, shooting, or stabbing pain, muscle cramps, lancinating pain, allodynia (when a pain from a stimulus that normally provokes pain does not provoke pain), hyperalgesia, and loss of proprioception also are possible (Corbett, 2005; Stillman & Cata, 2006). Neuropathic pain may be a consequence of CIPN; however, CIPN is not often assessed as a unique component of the chemotherapy experience (Binner et al., 2011). Every patient who reports numbness and/or tingling in the upper or lower extremities also should be assessed for neuropathic pain. The letters PQRST stand for a well-known mnemonic that can be used to assess any type of pain (Ryan, 1996). Assessment of pain should include asking about: (P) Provocation—what seems to bring it on and relieve it? (Q) Quality—what words would describe it? (R) Region—where does it hurt and is it general or well localized? (S) Strength—how bad is it on a scale of 1–10? (T) Timing—how long does it last? Is it constant or intermittent? How long have you had it? Is there a certain time of day when you notice it the most?

Pharmacologic Management

Numerous guidelines for the pharmacologic treatment of neuropathic pain have been developed with a consensus that anticonvulsants, serotonin norepinephrine reuptake inhibitors, tricyclic antidepressants (TCAs), opioids, and topical lidocaine are good treatment options for neuropathic pain (Dworkin et al., 2010; Moulin et al., 2007; O’Connor & Dworkin, 2009), although clinical trials of patients with painful CIPN are lacking.

A neuropathic treatment and referral algorithm was developed by Smith et al. (2011) for use by advanced practice nurses when managing patients with cancer-related neuropathic pain in an outpatient setting. The drugs included in the algorithm were 5% lidocaine patch (with extending dosing from 12–18 hours) for well-localized pain; gabapentin with an opioid as first-tier medications; and methadone, duloxetine, pregabalin, and nortriptyline as second-tier medications. Second-tier medications should only be prescribed after the patient has been referred to a neuropathic pain specialist. A two-institution prospective study found that neuropathic pain management improved over time when the algorithm was used (Smith et al., 2011). Advanced practice nurses are encouraged to refer to these guidelines when managing CIPN-related neuropathic pain. Studies of neuropathic pain in patients with cancer indicate that medications including gabapentin, pregabalin, amitriptyline, and duloxetine, which have been used successfully for neuropathic pain in patients without cancer, also may work for pain associated with CIPN (Kautio, Haanpaa, Saarto, & Kalso, 2008; Smith et al., 2012; Tsavaris et al., 2008).

Anticonvulsants

Anticonvulsants, including gabapentin and pregabalin, are frequently prescribed for neuropathic pain. The mechanism of action is unknown; however, they may work by affecting the transport of amino acids across neuronal membranes and stabilizing those membranes by binding to voltage-gated calcium channels (Dworkin et al., 2010). The starting dose for gabapentin is 100–300 mg at bedtime or three times daily. This dose can be increased as tolerated to a maximum dose of 3,600 mg per day. The starting dose for pregabalin is 50 mg three times daily or 75 mg twice daily, and can be increased as tolerated to a maximum dose of 600 mg per day. Anticonvulsants can produce dose-dependent dizziness and sedation (Dworkin et al., 2007, 2010; Tsavaris et al., 2008). Carbamazepine and lamotrigine also are anticonvulsants that may be used for treatment of neuropathic pain (Corbett, 2005).

Tricyclic Antidepressants

TCAs also may be used for management of neuropathic pain (Moulin et al., 2007). These drugs potentiate the effect of serotonin

Exploration on the Go

The Quick DASH outcome measure tool is available online for peripheral neuropathy assessment. To access, open a barcode scanner on your smartphone, take a photo of the code, and your phone will link automatically. Or visit www.dash.iwh.on.ca/system/files/quickdash_questionnaire_2010.pdf.
and norepinephrine in the central nervous system (CNS). Although TCAs are inexpensive and can be administered once daily, they invoke anticholinergic adverse effects including dry mouth, orthostatic hypotension, constipation, and urinary retention (Dworkin et al., 2010). Amitriptyline (a TCA recommended for neuropathic pain) should be started at a dose of 25 mg daily at bedtime and increased to 100 mg per day as tolerated. The starting dose for nortriptyline is 25 mg at bedtime and can be increased by 25 mg daily every three to seven days as tolerated up to a maximum dose of 150 mg per day (Dworkin et al., 2007).

Selective Serotonin Reuptake Inhibitors

Selective serotonin reuptake inhibitors work by selectively inhibiting the reuptake of serotonin in the CNS. This class of drugs reportedly has fewer side effects than TCAs; however, they might be less effective in the management of painful diabetic neuropathy (Corbett, 2005). Citalopram is initially started at a dose of 20 mg per day and is generally increased to a dose of 40 mg per day. Some early trials have shown modest benefits for citalopram; however, studies of analgesic efficacy remain inconsistent in the literature. A randomized, controlled trial found significantly greater pain relief with escitalopram compared with placebo (Dworkin et al., 2010). Escitalopram can be started at 10 mg per day and increased after one week to 20 mg per day.

Selective Serotonin Norepinephrine Reuptake Inhibitors

Selective serotonin norepinephrine reuptake inhibitors act by inhibiting serotonin and norepinephrine reuptake in the CNS where both antidepressant and pain inhibition are mediated. Duloxetine has demonstrated efficacy in painful diabetic peripheral neuropathy, and has been demonstrated to relieve pain related to CIPN (Smith et al., 2012). The starting dose should be 30 mg once daily and increased to 60 mg once daily after one week with patient tolerance to a maximum dose of 60 mg twice daily. The most common side effect associated with duloxetine is nausea, which can be minimized by gradual dose escalation (Dworkin et al., 2010). Venlafaxine has been
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studied in painful diabetic neuropathy and painful polyneuropathies of different origins. The starting dose for venlafaxine is 37.5 mg once or twice a day and can be increased by 75 mg each week to a maximum dose of 225 mg per day. Venlafaxine should be prescribed with caution for patients with a history of cardiac disease (Dworkin et al., 2007). Side effects associated with venlafaxine are mainly gastrointestinal in nature (Attal et al., 2010).

Topical Agents

Lidocaine produces local anesthesia by inhibiting the transport of ions across neuronal membranes, preventing initiation and conduction of normal nerve impulses. The 5% lidocaine patch can be applied daily to painful areas starting with 12 hours on and 12 hours off up to a maximum of three patches daily with a 12-18 hour maximum time on. The most common adverse effect associated with lidocaine patches are mild local reactions (Dworkin et al., 2007).

Capsaicin is derived from the main capsaicinoid in chili peppers and may deplete and prevent the reaccumulation of substance P, which is responsible for transmitting painful impulses from peripheral sites to the CNS. Application site reactions such as erythema are the most common adverse effects; however, long-term effects of use are currently unknown (Dworkin et al., 2010).

Upper Extremity Symptoms

Consequences of CIPN also include progressive neuromuscular weakness, which ultimately results in difficulty or inability to perform tasks of daily living and can affect quality of life (Lexell, 2000). Muscular weakness in the upper extremities negatively affects the ability to perform fine motor skills such as writing or dressing, reducing independence, or compromising the ability to perform job-related activities. Even so, little research exists to denote the effects of CIPN on the upper extremities; a great need remains for research in the neuromuscular consequences of CIPN to understand the underlying mechanisms by chemotherapy drug classification, dosing schedule, and interaction with comorbid illness. Although no evidence-based intervention exists to prevent or ameliorate neuromuscular weakness associated with CIPN, physical activity can assist in relieving weakness, restoring strength, and limiting compromises in physical functioning (Lexell, 2000). Although upper extremity weakness resulting from neurotoxic chemotherapy is not well characterized or understood, the inability to recruit or activate motor units may be the underlying mechanism.

Upper extremity manifestations of CIPN are not as common as sensory or motor deficits in the lower extremities. Consistent with nursing assessment processes, the first step in determining the presence and severity of upper extremity involvement from CIPN is to specifically inquire about symptoms related to upper extremity involvement. Symptoms need to be assessed at each visit, particularly if new or continuing treatment with neurotoxic agents is planned. Muscle strength and endurance are directly related to upper extremity physical functioning and performance, with muscle weakness and fatigue presenting with neurologic deficits (Visovsky, 2006). Symptoms related to arm weakness can be manifested as forearm fatigue upon

Dressing and Grooming
- Use zip pull and buttons, elastic shoe laces, Velcro® straps, orthotic inserts for shoes and slippers, and lightweight dressing sticks to put on garments without bending.
- Wear closed-toed shoes that fit well, gloves and warm socks in cold weather, and jewelry that does not require fastening.
- Avoid walking barefoot and wearing socks that are slippery or have seams.
- Break in new shoes gradually.

Lighting
- Keep rooms well lit.
- Place a lamp near the room entrance and keep the light switch visible and not covered by other items.
- Illuminate all stairs and hallways prior to entering.
- Keep a night light in the bedroom and bathroom or keep a flashlight with you or within reach to use when lighting is not adequate. Use a key chain with a light to help you see keyholes.

Stairs and Flooring
- Always use handrails and cover stairs with a nonslip surface.
- Clear stairways and hallways of objects and clutter.
- Paint the stairs in a light color for easier visibility; floors should have nonglare and nonskid surfaces.
- Avoid use of area rugs, tape or tack down carpet edges securely, and avoid surface drops between the carpet and other flooring.
- Wipe up spills and liquids immediately.

Bedroom
- Do not use chairs, tables, nightstands, or over-bed tables with wheels.
- Clear small area rugs, clothes, shoes, and clutter from walkways through your bedroom.
- If you use extension cords, secure them with electric tape along the edge of the floor.
- Remove furniture with sharp edges or corners.

Kitchen
- Area rugs near the sink should have nonslip backing.
- Use rubber gloves to wash dishes; check the water temperature with a nonbreakable thermometer and make sure it is below 110°F.
- Use lightweight, nonbreakable glasses, utensils, and plates.
- Shield your fingers when cutting foods.
- Open jars or soda cans with easy jar openers or grippers.
- Use pot holders and oven mitts to handle hot kitchen items.

Outside
- Absorb oil spills with sand or cat litter.
- Store rakes, shovels, and other garden equipment off the floor.
- Place nails, screws, and other hardware in containers with covers.
- Keep walkways clear of clutter.
- Always wear rubber shoes or work boots when you work in the garage or garden.

FIGURE 2. Safety and Adaptive Measures for Patients With Chemotherapy-Induced Peripheral Neuropathy

Note: Based on information from Almadrones & Arcot, 1999; Oklahoma State Department of Health, 2012; Wickham, 2007.
lifting, decreased grip strength, and difficulty with fine motor skills. In addition, determining whether the etiology of upper extremity weakness is the result of CIPN or is interrelated to other cancer treatments (e.g., mastectomy, radiation to the axilla or upper chest area) or complications of cancer treatment (e.g., lymphedema) may be difficult.

Fine Motor Skills and Functional Assessment

Assessment of suspected CIPN of the upper extremities consists of subjective symptom assessment, fine motor skill assessment, and assessment of upper extremity and grip strength. Subjective symptoms can be determined by asking whether the patient is experiencing numbness, tingling, or pain in the fingertips, hand, or upper arm, as well as the presence of any obvious motor deficits such as a decrease in grip strength with daily activities (e.g., being able to lift or grasp a coffee cup).

Standardized instruments also are available for this type of assessment, and although they are more comprehensive, the cost usually is minimal. The 30-item Disabilities of Arm, Shoulder, and Hand (DASH) tool developed by the American Academy of Orthopedic Surgeons is a self-report measure of upper extremity symptoms and the perceived ability to perform associated common activities. DASH is scored from 1-5, with higher scores equaling greater disability (Beaton et al., 2001).

Some simple, objective, clinical tests of fine motor skill and coordination that can be easily used and tested in the clinical setting are assessment of the ability to button and zip clothing, the ability to thread a large-bore needle, and the ability to perform handwriting. If the patient has difficulty with such tasks, a more formal assessment of fine motor functioning by a physical or occupational therapist, or an advanced practice nurse, may be indicated. Fine motor skills can be tested using the standardized Perdue Pegboard test. The Perdue Pegboard test measures gross movements of hands, fingers, and arms, as well as fingertip dexterity using sequential pegboard insertion of pegs and assembly of pegs, collars, and washers. Referral to a physical therapist also can be made for grip strength assessment. To assess grip strength, patients are instructed to squeeze the instrument using maximal effort. Three trials are typically used for this assessment and a mean score is calculated. If deficits are observed, referral to physical and/or occupational therapy and an assessment of home safety including instituting safety precautions for ischemic or thermal injury prevention may be necessary. Home safety recommendations and tips to help patients adjust to physical limitations can be found in Figure 2.

Lower Extremity Symptoms

Neuropathies of the lower extremities include numbness, tingling, neuropathic pain, leg weakness, and loss of proprioception. Although upper extremity symptoms affect fine motor

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skills, lower extremity symptoms affect gross motor skills that can impair functional status and reduce independence. Reduced proprioception combined with numbness increases the risk of falls and injury. In particular, reduced lower extremity proprioception may cause a misjudgment of foot position, increasing the risk of fall (Grewal et al., 2012).

Functional assessment of lower extremity function should be performed on every patient with lower extremity neuropathy. Evaluating gait and balance should begin by observing the patient walk naturally and taking note of any gait patterns that appear abnormal, as well as assessing gait speed and unsteadiness (Iqbal, 2005). Additional gait evaluations can be performed quickly with minimal need for additional equipment. Table 1 provides a description of gait and balance tests that take a minute or less each to perform and do not require any special equipment. Maintaining a safe environment and avoiding falls and injuries are a major focus of nursing care for patients with CIPN, particularly when the lower extremities are affected. A cane, walker, or wheelchair should be provided when balance is affected and fall is a concern.

Physical and Occupational Therapy

Physical and occupational therapy are important interventions to offer patients with lower extremity neuropathy. Physical therapists can assist patients with exercises that strengthen weak muscles and improve balance, and increasing evidence indicates that exercise improves functional status in patients with neuropathy (Allet et al., 2010; Asensio-Pinilla, Udina, Jaramillo, & Navarro, 2009; Kruse, Lemaster, & Madsen, 2010). Physical therapists also may suggest unique therapies such as monochromatic infrared photo energy and nerve stimulation that, although empirical evidence is inconclusive at this point, may benefit specific patients (Harkless, DeLellis, Carnegie, & Burke, 2006; Liu, Hsu, Lu, Chen, & Liu, 2010). Occupational therapists can help patients achieve their maximum performance status, as well as adapt to and compensate for physical challenges (Longpré & Newman, 2011). Organizations that provide supervised activity, including balance training, or other supportive services within local communities are described in Table 2.

Conclusions

CIPN resulting from disease progression and cancer treatment remains a significant problem for patients and clinicians alike. Assessment of the upper and lower extremities using simple, clinical testing can help identify CIPN early. Management of neuropathic pain and rehabilitative strategies to maximize physical functioning are the key components of management of CIPN. This algorithm provides the oncology nurse with appropriate clinical assessments that are both feasible and valid for obtaining such data and recommending useful interventions.

References

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