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

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Abstract

Oncology nurses play a critical role in assessment and management of chemotherapy-induced peripheral neuropathy. 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, we 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.

Introduction

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, bortizomib, and interferon. CIPN results in diverse symptom patterns and can lead to physical distress from neuropathic pain, as well as emotional distress, decrease in functional ability and social role impairment (Bakitas, 2007; Tofthagen, 2010).

Pre-existing conditions may predispose patients to develop neuropathy, including diabetes, alcoholism, amyloidosis, human immunodeficiency virus (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 it progresses (Visovsky, 2003).

While 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 clinical common assessment techniques, or gross grading scales.

Oncology nurses play a critical role in assessment and management of CIPN. Research has demonstrated that while nurses recognize the importance of assessing for CIPN, many lack confidence in their assessment skills (Binner, Ross, & Browner, 2011). Neurologic exams 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, we 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. 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 is also an important aspect of caring for these patients. The guidelines presented here are not meant as a substitute for evaluation and treatment by a neurologist. Instead, suggestions regarding assessment parameters that 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 are provided.

Initial Screening

Numbness and/or tingling in the distal extremities is considered the hallmark of CIPN and are consistently reported by patients with neuropathy (Tofthagen, 2010). Patients are often hesitant to report neuropathy because of a variety of reasons including fear of discontinuation of potentially lifesaving 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). Additionally, even though neuropathic pain can be 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 these reasons, it is important for clinicians to 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 more assessment is needed. If numbness, tingling or discomfort is affirmed, the next step is to ask a series of three questions regarding; 1) neuropathic pain 2) upper extremity loss of sensation and 3) 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). Diagnosing and managing cancer-related neuropathic pain is challenging and often results in inadequate pain management (Smith et al., 2011). Neuropathic pain is often describes as burning, shooting, or stabbing but muscle cramps, lancinating pain, allodynia, hyperalgesia, and loss of proprioception are also possible (Corbett, 2005; Stillman & Cata, 2006). Neuropathic pain may be a consequence of CIPN, however, it 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 should also 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). To review, the letters in the mnemonic stand for provocation, quality, region, strength, and timing. 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 re-uptake inhibitors, tricyclic antidepressants, opioids, and topical lidocaine are good treatment options for neuropathic pain although clinical trials in persons with painful CIPN are lacking (Dworkin, et al., 2010; Moulin et al., 2007; O'Connor & Dworkin, 2009).

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 to 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. Advanced practice nurses are encouraged to refer to these guidelines when managing CIPN related neuropathic pain. Studies of neuropathic pain in persons with cancer indicate that medications including gabapentin, pregabalin, amitriptyline, and duloxetine, which have been used successfully in non-cancer patients with neuropathic pain, 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 transportation of amino acids across neuronal membranes and stabilizing these membranes by binding to voltage gated calcium channels (Dworkin, et al., 2010). Gabapentin starting dose is 100–300mg at bedtime or three times daily. This dose can be increased as tolerated to a maximum dose of 3600mg per day. Pregabalin starting dose is 50mg three times daily or 75mg twice daily and can be increased as tolerated to a maximum dose of 600mg per day. Anticonvulsants can produce dose dependent dizziness and sedation (Tsavaris, et al., 2008) Dworkin et al., 2007; Dworkin et al., 2010). Carbamazepine and lamotigine are also anticonvulsants that may be used for treatment of neuropathic pain (Corbett, 2005).

Tricyclic Antidepressants (TCAs)

The TCAs also may be utilized for management of neuropathic pain (Moulin, et al., 2007). These drugs potentiate the effect of serotonin and norepinephrine in the central nervous system (CNS). While 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, which is one TCA recommended for neuropathic pain, should be started at 25mg/daily and bedtime and increased to 100mg/day as tolerated. Nortriptyline starting dose is 25mg at bedtime and can be increased by 25mg daily every 3–7 days as tolerated up to a maximum dose of 150mg per day (Dworkin et al., 2007).

Selective Serotonin Reuptake Inhibitors (SSRIs)

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

Selective Serotonin Norepinephrine Reuptake Inhibitors (SSNRIs)

SSNRIs 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 recently been demonstrated to relieve pain related to CIPN (Smith, et al., 2012). Starting dose should be 30mg once daily and increased to 60mg once daily after one week with patient tolerance to a maximum dose of 60mg 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 studied in painful diabetic neuropathy and painful polyneuropathies of different origins. The starting dose for venlafaxine is 37.5mg once or twice a day and can be increased by 75mg each week to a maximum dose of 225mg per day. Venlafaxine should be prescribed with caution in

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 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 re-accumulation of a 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, there is little research denoting the effects of CIPN on the upper extremities. There remains a great need for research in the neuromuscular consequences of CIPN in order to understand the underlying mechanisms by chemotherapy drug classification, dosing schedule and interaction with comorbid illness. While there is no evidence-based intervention to prevent or ameliorate neuromuscular weakness associated with CIPN, physical activity can assist in relieving weakness, restore strength, and limit compromises in physical functioning (Lexell, 2000). While 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 Symptoms

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 determine 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, especially 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 lifting, decreased grip strength, and difficulty with fine motor skills.

Additionally, it may be difficult to determine if the etiology of upper extremity weakness is the result of CIPN, or is inter-related to other cancer treatments such as mastectomy or radiation to the axilla or upper chest area, or complications of cancer treatment such as lymphedema.

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 if 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 such as being able to lift or grasp a coffee cup. Standardized instruments are also available for this type of assessment, and although are more comprehensive, the cost is usually 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 that is scored 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 hand writing. If the patient has difficulty with such tasks, a more formal assessment of fine motor functioning may be indicated. Fine motor skills can be tested using the standardized Perdue Pegboard test (North Coast Medical, Morgan Hill, CA). The Perdue Pegboard test measures gross movements of hands, fingers and arms, and “fingertip” dexterity using sequential pegboard insertion of pegs and assembly of pegs, collars, and washers. Referral to a physical therapist can also 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 Table 1. The majority of this information comes from an educational pamphlet originally developed by Amadrones and Arcot (1999), published by Memorial Sloan Kettering Cancer Center and also previously published in the Oncology Nursing Forum.

Lower Extremity Symptoms

Neuropathies of the lower extremities include numbness, tingling, neuropathic pain, leg weakness, and loss of proprioception. While upper extremity symptoms affect fine motor skills, lower extremity symptoms affect gross motor skills, which 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 with observing the patient walk naturally and taking note of any gait patterns that appear abnormal, gait speed, and unsteadiness (Iqbal, 2012). Additional gait evaluations can be performed quickly with minimal need for additional equipment. Table 2 provided a description of gait and balance tests, which take a minute or less each to do and do not require any special equipment. Maintaining a safe environment, and avoiding falls and injuries is a major focus of nursing care for persons with CIPN, especially when the lower extremities are affected (Table 1). 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 there is increasing evidence indicating that exercise improves functional status in persons with neuropathy (Allet et al., 2010; Asensio-Pinilla, Udina, Jaramillo, & Navarro, 2009; Kruse, Lemaster, & Madsen, 2010). Physical therapists may also suggest unique therapies such as monochromatic infrared photo energy and nerve stimulation, which although empiric evidence is inconclusive at this point, may benefit specific patients (Harkless, DeLellis, Carnegie, & Burke, 2006; Liu, Hsu, Lu, Chen, & Liu, 2010). Occupational therapists can assist 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 3.

Conclusions

Chemotherapy-induced peripheral neuropathy resulting from disease progression and cancer treatments 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.

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Figure 1.
Algorithm for Nursing Assessment and Management of Chemotherapy-Induced Peripheral Neuropathy

Table 1

Safety and adaptive measures.

Dressing and Grooming	Use zipper pulls and buttoners. Elastic shoe laces. Velcro straps. Orthotic inserts for shoes and slippers. Lightweight dressing sticks to put on garments without bending. Wear closed toed shoes that fit well. Wear gloves and warm socks in cold weather. Wear jewelry that does not require fastening. Avoid walking barefoot. Break in new shoes gradually. Wear thick, soft socks avoiding socks that are slippery or have seams.
Lighting	Keep room well lit. Place lamp near room entrance. Keep light switch visible and not covered by other items. Illuminate all stairs and hallways prior to entering. Keep a nightlight in the bedroom and bathroom 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 on stairs. Cover stairs with a non-slip surface. Paint the stairs in a light color for easier visibility. Clear stairways and hallways of objects and clutter. Floors should have non-glare and non-skid surfaces. Avoid use of area rugs. Tape or tack down carpet edges securely. Avoid surface drops between a 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, stools, 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.
Bathroom	Bathtub or sink area rugs should have non-slip backing. Use non-skid strips or mats in tub or shower. Use portable hand grips over the tub or install shower grips Set water thermostat below 110 degrees F and check water temperature with a non-breakable thermometer. Use a liquid soap dispenser, soap on a rope, or a washcloth to hold your soap. Avoid slippery, wet floors. Wipe up liquids immediately.
Kitchen	Area rugs near the sink should have non-slip backing. Use rubber gloves to wash dishes Check water temperature with a non-breakable thermometer and make sure water temperature is below 110 degrees F. Use light-weight, non-breakable 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 kitty 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.

(Almadrones & Arcot, 1999; Oklahoma State Department of Health, 2012; Wickham, 2007)

Table 2

Evaluation of balance.

Test	Directions	Interpreting Results
Timed Up and Go(Podsiadlo & Richardson, 1991; Shumway-Cook, Brauer, & Woollacott, 2000)	Place an arm chair on one side of the room and a piece of tape on the floor 10 feet away from the chair. Instruct the patient to stand up, walk to the line on the floor, turn around and walk back to the chair then sit back down, walking at their regular pace.	Scores under 10 seconds are considered normal. Times >14 seconds indicated a high risk of falls.
Romberg Test(Notermans, van Dijk, van der Graaf, van Gijn, & Wokke, 1994)	Have patient a) stand with feet approximately 6–8 inches apart with hands at their sides and close their eyes. Time how long it takes for them to open their eyes or feel as if they will lose their balance. If patient can perform for 60 seconds without difficulty b) have patient perform with feet close together and eyes closed.	Inability to maintain balance for at least 60 seconds with feet together indicates ataxia.
Sharpened Romberg(Sarabon, Mlaker, & Markovic, 2010)	Have patient stand in tandem position (one leg in front of the other) with hands sides and eyes closed. Time how long it takes for them to open their eyes or feel as if they will lose their balance.	Times <30 seconds indicate increased fall risk.
Unipedal Stance Time (Hurvitz, Richardson, & Werner, 2001)	Have patient stand on one foot, unsupported, for as long as possible. Allow 3 tries.	Times <45 seconds indicate increased fall risk.

Table 3

Community-Based Resources for Persons with CIPN.

Organization	Services	Website	Email address	Phone
Livestrong at the YMCA	Free 12 week program, led by trained fitness instructors, for cancer survivors that helps, increase flexibility and endurance and improve strength and functional ability and minimize side effects. Offered in many states in the Eastern United States, and the Midwest, Washington, and Idaho	http://www.livestrong.org/What-We-Do/Our-Actions/Programs-Partnerships/LIVESTRONG-at-the-YMCA	YMCA@LIVESTRONG.org	800-872-9622, ext 2847
Gentiva Safe Strides	Home based balance training program for adults >65 that have balance problems from any cause, including peripheral neuropathy. Provider referral needed.	http://www.gentiva.com/patients_caregivers/gentiva_safe_strides/	Varies	1-888-GENTIVA
The Neuropathy Association	Support groups that meet in various locations throughout the nation and educational materials available online and	http://www.neuropathy.org	info@neuropathy.org	212-692-0662