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CASE STUDIES IN THE MANAGEMENT OF NEUROPATHIC PAIN IN OLDER PATIENTS

INTRODUCTION

Neuropathic pain, defined by the International Association for the Study of Pain as that initiated or caused by a primary lesion or dysfunction in the nervous system,[1] occurs in approximately 1.5% of the U.S. population.[2] Most research into the mechanisms and treatment of neuropathic pain has examined postherpetic neuralgia and diabetic peripheral neuropathy[3]—2 types of neuropathic pain that commonly occur in older adults.[4-6]

Multiple complex mechanisms originating from the central or peripheral nervous system are involved in generating or sustaining neuropathic pain (Table),[7,8] and it is likely that potentially overlapping pain mechanisms coexist in an individual patient.[9] Consequently, symptoms vary between patients and patients' responses to neuropathic pain treatments can vary as well. Further, most neuropathic pain conditions are largely resistant to treatment with commonly prescribed analgesics.[10] Neuropathic pain is therefore universally accepted as the most difficult type of pain to treat[9,11]; however, until recently, evidence-based guidelines for treatment of neuropathic pain have not been available.

Most neuropathic pain conditions are largely resistant to treatment with commonly prescribed analgesics

Within the past 2 years, evidence-based recommendations for treatment of neuropathic pain were developed by a committee of the Fourth International Conference on the Mechanisms and Treatment of Neuropathic Pain, based on a systematic review of the literature and the guideline authors' collective clinical experience.[3] In addition, a specific guideline for treatment of postherpetic neuralgia was published by the American Academy of Neurology.[12] Based on the first-line recommendations from these evidence-based guidelines, this newsletter uses case studies to illustrate the assessment and management of neuropathic pain.

TABLE

NEUROPATHIC PAIN MECHANISMS AND SYNDROMES

MECHANISMS*	SYNDROMES†
Peripheral nervous system	
• Collateral sprouting	• Chemotherapy-induced neuropathy
• Increased damaged axon and sprout activity	• Complex regional pain syndrome
• Peripheral neuron sensitization	• Diabetic neuropathy
• Sympathetic postganglionic fiber invasion of dorsal root ganglia	• HIV sensory neuropathy
• Unmasking of silent nociceptors	• Neuropathy secondary to tumor infiltration
	• Phantom limb pain
	• Postherpetic neuralgia
	• Postmastectomy pain
	• Trigeminal neuralgia
Central nervous system	
• Central neuron hyperexcitability (central sensitization)	• Central poststroke pain
• Disinhibition-removal of tonic descending inhibitory activity	• Multiple sclerosis pain
• Reorganization of synaptic connectivity	• Parkinson's disease pain
	• Spinal cord injury pain

*Adapted from Gordon DB, Love G. Pharmacologic management of neuropathic pain. *Pain Management Nursing.* 2004;5(suppl 1):19-33 with permission from Elsevier.

†Adapted from Dworkin RH. An overview of neuropathic pain: syndromes, symptoms, signs, and several mechanisms. *Clin J Pain.* 2002;18:343-349 with permission from Lippincott Williams & Wilkins.

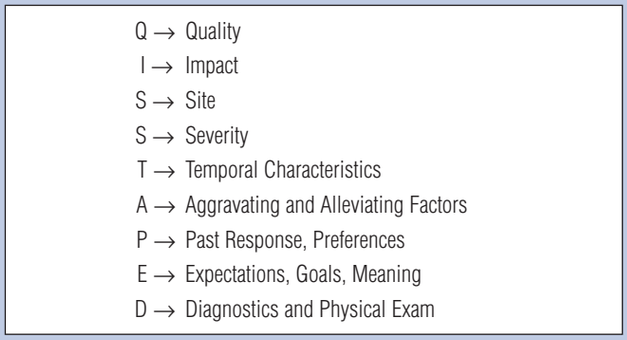
NEUROPATHIC PAIN ASSESSMENT

Because the exact relationship between neuropathic pain mechanisms and symptoms remains unclear[10] and the severity of pain often does not correlate with the extent of tissue damage,[8] neuropathic pain often goes undiagnosed and untreated.[10] Given the lack of a definitive diagnostic test for neuropathic pain, and the potential for significant interpatient variability in presentation, obtaining a comprehensive and focused history and clinical evaluation are essential to appropriate diagnosis and treatment.[13] The history and physical examination should focus on identification of comorbid conditions; assessment of somatosensory function, including presence of positive (eg, paresthesia, hyperalgesia) and negative (ie, sensory loss) sensory signs; and evaluation of spontaneous versus stimulus-evoked pain, as well as onset, location, and distribution of pain.[13] Specific assessment tools, such as the Neuropathic Pain Scale (NPS)[14] or Neuropathic Pain

Questionnaire (NPQ),[15] can be used to evaluate the quality or intensity of neuropathic pain.[13,16] It is also important to evaluate the outcome of any previous treatments and determine whether the medications were properly titrated (ie, until pain relief was achieved or unacceptable side effects occurred).[13] Finally, the impact of pain on the patient's quality of life and the patient's therapeutic goals should be defined (Figure).[13,16]

FIGURE

PAIN ASSESSMENT MNEMONIC: QISS TAPED



Herr K. Neuropathic pain: a guide to comprehensive assessment. *Pain Management Nursing.* 2004;5(suppl 1):9-18. Mnemonic adapted with permission from M. Backonja, MD.

This evaluation process may be further complicated in older patients who can present with additional barriers to accurate pain assessment because of their inability or reluctance to accurately report pain.[17] The presence of sensory or cognitive impairment, common among frail older adults, can make communication more difficult. Other issues that may affect pain identification in older adults include fear of addiction, fear of being labeled a "bad patient," fear of being diagnosed with a serious disease, and reluctance to report pain symptoms that the patient fears may not be believed by caregivers and healthcare providers.[18]

Older patients can present additional barriers to accurate pain assessment because of their inability or reluctance to accurately report pain

Case 1 Assessment: *Patient 1 is female, aged 86 years, with new onset foot pain. Her medical history revealed noninsulin-dependent diabetes mellitus that had been well controlled with diet, weight control, and oral agents for 5 years, and hypertension treated with hydrochlorothiazide. She has been using an over-the-counter (OTC) product to treat insomnia 2 to 3 times weekly, when the pain interfered with her ability to sleep at night. Distractions provided by television and foot rubs were occasionally helpful. She described her pain as "burning," "tingling," and "annoying," and rated the intensity as 2 to 3 on scale of 0 to 10, increasing as the day progressed to a high of 4/10 at bedtime. The physical exam revealed no skin breakdown or lesions, toenails that were somewhat brittle but in good condition, and good capillary refill. Peripheral pulses were palpable, there was no clinically evident reduction in sensation to light touch, pin prick, vibration, or cold stimulus, no allodynia, and deep tendon reflexes were 1+ and symmetrical.*

Case 2 Assessment: *Patient 2 is male, aged 72 years, with neuralgia paresthetica (lateral femoral cutaneous neuralgia) diagnosed after undergoing total hip arthroplasty. His general health was good, with no history of other neurologic disorders, and he was fully ambulatory after recovery from surgery and rehabilitation. He described his pain as "burning," and rated the severity as 4 to 7 on a scale of 0 to 10, with higher scores when engaging in activities, but could not identify obvious precipitating or relieving factors. The pain was interfering with enjoyment of most activities, including household chores, recreation, and sex. Transient relief had been achieved with a nerve block; however, he did not want further surgical or invasive interventions. The physical exam revealed a typical pattern of sensory disturbance along the affected antero-lateral thigh region, described as feeling like "scalded skin." Percussion medial to the anterior superior iliac crest caused paresthesia and exacerbated the pain; however, there was no allodynia or hyperalgesia along the cutaneous nerve distribution.*

Case 3 Assessment: *Patient 3 is female, aged 75 years, with postherpetic neuralgia resulting in severe, unrelenting pain in the right side T-4 dermatome, which persisted following a case of shingles that occurred 2 years ago. Her medical history revealed arthritis treated with celecoxib 200 mg/day and she had used both hydrocodone/ and oxycodone/acetaminophen combination products in the past, but worried about "addiction" and had experienced opioid-related bowel dysfunction. Her medication history also included previous use of amitriptyline, which had resulted in confusion and other intolerable side effects. She described her pain as continuous, with episodes of sharp, shock-like sensations ("like electricity"), and circled the highest pain level on the Pain Thermometer tool, which she said she understood. Her pain interfered with all activities, social interests, and sleep. She also reported being "very depressed" and was tearful and somewhat withdrawn during the interview; she was being treated with citalopram 10 mg daily. Examination revealed a thin, frail woman with well-healed scarring in the right T-4 dermatomal distribution, and marked allodynia to light touch in this region. She pleaded not to be examined any more.*

Meeting Patient Needs

An important component of an initial pain assessment process is to discuss the patient's therapeutic goals and expectations.[17] Adequate pain relief has been described as that which: allows restful sleep; offers sufficient relief at rest to permit engagement in social and recreational activities; allows tolerable pain with activity to permit normal function; and does not alter mood or cognition.[18] When selecting medication for management of neuropathic pain, factors such as previous medication experience, health status, sleep disturbance, and pain chronicity should be considered.[8] The clinician should also evaluate the balance of benefits versus risks for various interventions, as well as the period of trial and error when new medications will be initiated and titrated.[17] Potential treatment side effects should be openly communicated and appropriately managed if they occur. Finally, although the complex nature of persistent pain often makes complete pain elimination unrealistic, functional improvements and reduction in pain

may be achieved in many patients.[17] Open communication between the patient and provider is therefore essential in establishing realistic patient expectations and is an important element in the development of successful treatment plans.

Initial pain assessment should include the patient's therapeutic goals and expectations

Case 1 Patient Expectations: *The therapeutic goal of patient 1 was for pain relief to be sufficient to allow improved sleep.*

Case 2 Patient Expectations: *Patient 2 described several therapeutic goals related to improving his quality of life: to achieve sufficient relief throughout the day to permit him to "get on with life," play golf, enjoy his family, take care of his yard, and to be able "to sit still for more than a minute without having to jump up and down like a jack-in-the-box."*

Case 3 Patient Expectations: *The therapeutic goal of patient 3 was to achieve at least a 30% reduction in pain, which she believed would allow her to feel that "life is worth living again."*

TREATMENT CHALLENGES IN MANAGEMENT OF NEUROPATHIC PAIN IN OLDER ADULTS

Need for Rational Polypharmacy

Many of the challenges in the delivery of effective neuropathic pain relief in older adults are common to those in effective management of any pain syndrome in this population. Adding to the complexities described above, multiple comorbidities in older adults with neuropathic pain increase the risk of drug-disease interactions, and the polypharmacy which is often required increases the risk of drug-drug interactions.[3] In addition, pharmacokinetic and pharmacodynamic differences in older adults can contribute to increased sensitivity to potential adverse drug reactions (ADRs).[17] Unlike other pain syndromes, however, the potential for multiple interacting mechanisms and mediators involved in neuropathic pain[19] contributes to substantial variability in symptoms and treatment response between patients with the same diagnosis,[8] and rational polytherapy is often needed to achieve therapeutic goals for neuropathic pain.[8] Thus, individualized therapeutic trials are the hallmark of effective pharmacotherapy for neuropathic pain.[9]

Individualized therapeutic trials are the hallmark of effective pharmacotherapy for neuropathic pain in older adults

Minimizing Risk/Maximizing Benefit

To minimize the risk of these potential problems while maximizing therapeutic benefits, some basic therapeutic guidelines for the management of persistent pain in older adults should be considered. First, the least invasive and least toxic intervention or combination of interventions that provides relief for a specific pain condition should be employed.[17] In addition, the Fourth International Conference recommendations acknowledge that pharmacologic management is not curative, and should be considered an integral component of a comprehensive treatment regimen that includes nonpharmacologic therapies (eg, physical therapy, psychological treatments, invasive procedures) provided in a setting that includes education, support, and reassurance.[3] Finally, pharmacologic therapy should be individualized, with careful adjustments as necessary, based on frequent monitoring for efficacy, ADRs, and treatment compliance.[3]

PHARMACOLOGIC TREATMENT OPTIONS

Based on results of published trials and clinical experience, recommendations for first-line treatment options for management of neuropathic pain include the lidocaine patch 5%, gabapentin, tricyclic antidepressants (TCAs), tramadol, and opioid analgesics.[3] Although some of these agents are not Food and Drug Administration (FDA) approved for neuropathic pain, they are primarily used for this indication,[2] and may be appropriate choices for first-line treatment, depending on the individual patient. Other agents that have been evaluated and found effective in limited numbers of patients may be considered as second-line therapy or beyond, for the management of difficult-to-treat patients who are unresponsive or have contraindications to first-line agents.

Case 1 Treatment: *Use of an OTC "sleep aid" is not appropriate for this condition. After reevaluation of blood sugar control and treatment and advice about therapeutic footwear and ongoing foot care, consideration of a single drug that will reduce neuropathic pain and help initiate sleep should be sufficient to meet this patient's expectations and prevent further morbidity from inappropriate medication use and sleep deprivation. Low dose tramadol (12.5–25 mg), slow titration of a bedtime dose of gabapentin (ie, 100 mg increments), or a very low dose (10 mg) of a secondary amine TCA (eg, desipramine or nortriptyline) are among the numerous pharmacotherapeutic options.*

Case 2 Treatment: *Most commonly occurring in association with use of a restrictive belt (eg, "utility" belts worn by policemen, repairmen, etc.), often in association with abdominal obesity, which can result in traction or compression of the lateral femoral cutaneous nerve as it descends beneath the iliac crest, the cause of this neuropathic pain syndrome after hip arthroplasty is unknown. Weight reduction and education about nonrestrictive garments is always advised and nerve blocks may be helpful. Because other approaches were unsuccessful in this man's case, pharmacotherapy is clearly indicated. Slow upward titration of gabapentin to a dose of 800 mg 3 times daily over the course of several weeks was tolerated, with tramadol 50 mg, to use ½ to 1 tablet up to twice daily, as needed for breakthrough pain.*

Case 3 Treatment: *Rational polypharmacy that takes advantage of the synergistic or additive drug mechanisms at lower doses (with close monitoring for adverse effects and frequent follow-up visits until doses and outcomes are stable) is often indicated for cases like this. Application of the lidocaine patch 5% to cover the painful, but intact skin area affected is a good starting point. In addition, the patient's history of depression and problems with TCAs may have been the result of a dose of a tertiary amine that was too high; thus it would be reasonable to substitute an agent in another antidepressant drug class such as duloxetine (starting at 30 mg daily and increasing*

to 60 mg daily, if tolerated) instead of citalopram. If tolerated but insufficient to achieve pain treatment goals, then titration of an opioid analgesic would be a rational third step.

Topical Analgesics

When applied to intact skin, topical agents relieve peripherally generated localized pain via activity within the skin, soft tissues, and peripheral nerves directly underlying the site of application, without resulting in clinically significant serum drug levels.[20] Thus, topical agents possess a low potential for systemic side effects or significant drug-drug interactions.

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Lidocaine patch 5%

The lidocaine patch 5% is a targeted peripheral analgesic that acts by binding to sodium channels on damaged nociceptor and sensory nerve fibers, resulting in fewer abnormal action potentials and decreased pain.[21] In addition, the patch provides a physical barrier that shields the painful area from stimuli (eg, clothing) that can provoke local pain (ie, allodynia). Recommended as a first-line agent for treatment of neuropathic pain,[3,12] the efficacy of the lidocaine patch 5% has been demonstrated in randomized, vehicle-controlled trials.[22,23] It is the only FDA approved topical analgesic for the treatment of a neuropathic pain condition (ie, postherpetic neuralgia).[20] In addition to postherpetic neuralgia,[22-24] the lidocaine patch 5% has also been evaluated for use in refractory neuropathic pain of various origins[25,26] and in an open-label pilot study for treatment of diabetic neuropathy.[27] As a topical agent, the lidocaine patch 5% has not been associated with systemic side effects; mild and transient localized skin reactions (eg, erythema, edema, or abnormal sensation) are the most common ADRs reported in clinical trials.[26-28]

Other topical agents

Other topical agents that have been used for the treatment of patients with neuropathic pain include capsaicin, clonidine, doxepin, a eutectic mixture of local anesthetics (EMLA) (eg, containing lidocaine 2.5% and prilocaine 2.5%), a topical cream containing amitriptyline and ketamine, locally applied opioids, and a spray formulation of isosorbide dinitrate.[9] Although none of these agents have been consistently demonstrated to be effective in clinical trials and are not considered first-line agents for management of neuropathic pain,[3] they may occasionally be effective in individual patients.

Anticonvulsants

Anticonvulsants act by several different mechanisms, including, but not limited to, effects on sodium or calcium conductance, increases in gamma-aminobutyric acid, and decreases in glutamate; however, their exact mechanism of action in neuropathic pain relief remains unknown.[8] Several anticonvulsant agents have been used for the management of neuropathic pain; gabapentin,[29] carbamazepine, and pregabalin[29] have received FDA approval for specific neuropathic pain syndromes. Among these, gabapentin[3] and pregabalin[3,12] are recommended as first-line agents.

Several anticonvulsant agents have been used for the management of neuropathic pain

Gabapentin

Clinical trials have demonstrated the efficacy of gabapentin for the treatment of postherpetic neuralgia,[30,31] for which it is FDA approved.[29] In a trial evaluating its use in adults with postherpetic neuralgia, gabapentin reduced the daily average pain score 33.3% compared with placebo (7.7%) (P<.001).[30] It was generally well tolerated in a population (n=109) with an average age of 73 years,[30] with no higher incidence of central nervous system–related ADRs (ie, dizziness, somnolence, and ataxia) in the older vs younger study participants.[30] Gabapentin has also been shown in small clinical trials to be effective and well tolerated for treatment of neuropathic pain associated with other conditions, including diabetic peripheral neuropathy,[32] Guillain-Barré syndrome,[33] and phantom-limb pain.[34] Compared with other anticonvulsant agents used for treatment of neuropathic pain (eg, carbamazepine, lamotrigine), gabapentin has the advantage of being associated with fewer drug-drug interactions. Its half-life, however, can exceed 24 hours in some older patients, necessitating dosing reduction in patients with renal dysfunction, and it can take as long as 4 to 7 days to achieve steady-state concentrations.[35] The most common side effects associated with gabapentin are somnolence, ataxia, fatigue, and dizziness; less frequently reported effects include nystagmus, tremor, and diplopia.[36]

Other anticonvulsant agents

Carbamazepine's efficacy in the treatment of trigeminal neuralgia, for which it is FDA approved,[29] has long been established[37,38]; however, its efficacy in trials for other neuropathic pain conditions has been inconsistent.[3,36] Liver enzyme and CBC monitoring is required[36]; it induces CYP3A4 (accelerating the clearance of multiple drugs), and older adults are particularly susceptible to its adverse effects.[35] As such, carbamazepine has a less favorable safety and tolerability profile compared with gabapentin.[8] Carbamazepine is currently recommended as a second-line agent in those patients in whom an anticonvulsant is indicated who are not responsive to gabapentin.[3]

Pregabalin, a recently approved anticonvulsant for treatment of diabetic peripheral neuropathy and postherpetic neuralgia,[29] has been shown in placebo-controlled clinical trials to be effective for both of these neuropathic pain conditions.[39-44] Its adverse effect profile is similar to that of other central nervous system (CNS) depressants (eg, dizziness, somnolence, ataxia, confusion).[45] In clinical trials, pregabalin has been found to be generally well tolerated; however, one group of investigators reported that patients aged ≥ 65 years experienced adverse effects slightly more often than younger patients.[42] The Drug Enforcement Agency has proposed a schedule V classification for pregabalin because of its potential for physical dependence and subjective ratings of "drug high" similar to diazepam 30 mg.[46] There are no published trials comparing pregabalin with other agents, and there is no strong evidence that has demonstrated pregabalin has a clear advantage in efficacy or safety over other available treatments, although its side effect profile suggests it might offer advantages to older patients in terms of tolerability to TCAs and may have a more rapid onset of action than gabapentin.[44,45]

Other anticonvulsants that have been used for management of neuropathic pain syndromes include tiagabine, lamotrigine, oxcarbazepine, topiramate, and valproic acid. Because of the adverse side effects related to the CNS for the anticonvulsants, precautions related to fall prevention are warranted.

Antidepressants

Tricyclic antidepressants

TCAs were the first category of pharmacologic agents that proved effective for treatment of neuropathic pain, and are still considered first-line agents.[3,12] Although their analgesic mechanism of action remains unclear, they are believed to inhibit nociceptive pathways by blocking the reuptake of serotonin and norepinephrine.[36] In animal models of peripheral neuropathic pain, TCAs have been shown to act as sodium channel blockers, similar to local anesthetic agents. The efficacy of TCAs for management of postherpetic neuralgia and diabetic peripheral neuropathy was well documented a decade ago in a meta-analysis[47]; however, their adverse effect profile limits their usefulness in older adults.[3] TCAs can cause balance problems and cognitive impairment, as well as other anticholinergic effects, and should be used cautiously in patients with a history of cardiovascular disease, glaucoma, urinary retention, or autonomic neuropathy.[3] In addition, they should be avoided in patients with second- or third-degree heart block, arrhythmias, prolonged QT interval, or severe liver disease and those who have experienced a recent myocardial infarction.[8] A screening electrocardiogram is recommended before beginning treatment in patients aged > 40 years to check for cardiac conduction abnormalities, and TCAs should be used with caution in patients at risk of suicide or accidental death from overdose.[3] TCAs have the potential to interact with drugs metabolized by cytochrome P4502D6 (eg, cimetidine, phenothiazines, and class 1C antiarrhythmics) and they may block the effects of some antihypertensive drugs (eg, clonidine or guanethidine). Among the various TCAs, secondary amines (eg, nortriptyline, desipramine) are preferred because of a lower incidence of ADRs that are troublesome in older adults, such as sedation, postural hypotension, and anticholinergic effects.[8]

Tricyclic antidepressants were the first category of pharmacologic agents that proved effective for treatment of neuropathic pain

Other antidepressant agents

Clinical trials also indicate that citalopram[48] and paroxetine[49] (selective serotonin reuptake inhibitors), venlafaxine[50] and duloxetine[51] (serotonin and norepinephrine reuptake inhibitors), and bupropion[52] are effective for treatment of neuropathic pain. Selective serotonin reuptake inhibitors have fewer adverse effects and are generally better tolerated than TCAs, and these agents may therefore be recommended as second-line medications for patients intolerant of or nonresponsive to a TCA in whom another antidepressant is being considered.[3]

Tramadol

Tramadol is an oral analgesic with a dual mechanism of action: it inhibits neuronal reuptake of norepinephrine and serotonin and is a μ-opioid receptor agonist.[53] Found effective in clinical trials for management of diabetic peripheral neuropathy[54] and polyneuropathy,[55] tramadol is recommended as a first-line agent for treatment of neuropathic pain.[3] Like many of the drugs used for the management of neuropathic pain, however, tramadol is associated with several adverse effects which are troublesome in older adults, including dizziness, nausea, constipation, somnolence, orthostatic hypotension, and exacerbation of cognitive impairment.[3] Its use is also associated with an increased risk of seizures in patients with a history of seizures or those who are concurrently receiving drugs that can lower the seizure threshold (eg, antidepressants, opioids, or neuroleptics). Dosage adjustment is necessary in patients with renal or hepatic disease.[3] Except in patients with a history of substance abuse, tramadol has a low abuse potential compared with other opioid analgesics.[56] Because equivalent doses of morphine may be associated with a greater incidence of ADRs (especially constipation, neuropsychiatric symptoms, and pruritus), laxatives, antiemetics, and antipsychotics are required less frequently with tramadol—an important consideration in older patients.[35] Dosing for patients aged > 65 years should be initiated at the low end of the dosing range, and the total dose daily should be ≤ 300 mg for patients aged > 75 years.[29]

Opioid analgesics

Opioid analgesics are among the recommended first-line agents for treatment of neuropathic pain.[3,12] The efficacy of opioid analgesics for treatment of various neuropathic pain syndromes has been demonstrated in recent studies, including morphine in postherpetic neuropathy[57] and phantom limb pain[58]; oxycodone in postherpetic neuralgia[59] and diabetic neuropathy[60,61]; and methadone[62] and levorphanol[63] in various neuropathic pain syndromes. The most common ADRs associated with opioid analgesics are constipation, sedation, and nausea. In older adults, the occurrence of cognitive impairment and problems with mobility can contribute to an increased risk of falls resulting in fractures, thus careful monitoring and titration are essential.[3] As in other pain conditions, opioids should be used with caution in patients with a history of substance abuse or attempted suicide. Despite increasing acceptability of opioids in treatment of persistent pain syndromes, selected opioids should be used with caution in older adults. Methadone should be prescribed by those with considerable experience in monitoring the effects of its long half-life to avoid respiratory depression.[35] Propoxyphene[17] and meperidine[35] are not recommended for use with older adults due to the potential for neurotoxic metabolite accumulation.

The efficacy of opioid analgesics for treatment of various neuropathic pain syndromes has been demonstrated in recent studies

Case 1 Outcome: *Normal HgA1c levels indicated the patient was adhering to her diabetic therapy. She was counseled about the continuing importance of compliance to help prevent progression of peripheral neuropathy. Retinal exam and renal studies were normal; since there were no ocular or cardiac contraindications, she was prescribed nortriptyline 10 mg. She responded well, experiencing no confusion or ataxia or changes in bowel or bladder function at this dose. The patient reported that "a bit of cotton mouth first thing in the morning" was worth the relief and restful sleep.*

Case 2 Outcome: *"Baseline" pain was reduced by approximately 50% with gabapentin without untoward ADRs. He reported very rarely requiring tramadol, only on particularly "tough" days, or with pain flares. He hoped that his problem would spontaneously remit over time. Since his neuropathic pain was controlled and he had a new, otherwise painless, prosthetic hip, the patient was motivated to lose 15 to 20 pounds by walking an hour a day and reducing his caloric intake.*

Case 3 Outcome: *The patient reported that the lidocaine patch 5% was particularly helpful in controlling her stimulation-induced burning pain and ability to tolerate clothing. Her mood, sleep, and intensity and frequency of spontaneous shock-like pains improved with duloxetine, but she was unable to tolerate more than 30 mg daily due to nausea. Oxycodone (immediate-release) 5 mg tablets were prescribed, to be used every 3 to 4 hours as needed to control pain and improve function, along with a bowel regimen. After 2 weeks, she required an average of 4 tablets daily to keep her pain ≤ level 4, and she was switched to continuous release oxycodone, 10 mg every 12 hours, coupled with the nightly use of a senna compound to maintain regular bowel activity. Satisfied with this therapy, her family reported that she seemed "20 years younger."*

CONCLUSIONS

Assessment and treatment of neuropathic pain is difficult, and both are compounded in older patients who often have multiple comorbidities and diminished communication skills. While polytherapy is often indicated for management of neuropathic pain, extra caution is required in older adults because of an increased risk of drug-drug and drug-disease interactions. Neuropathic pain continues to be a treatment challenge; however, a thorough understanding of both the older and newer treatment options and evidence-based support for their use will hopefully improve rational pharmacologic management.

While polytherapy is often indicated for management of neuropathic pain, extra caution is required in older adults because of an increased risk of drug-drug and drug-disease interactions

Among the available pharmacologic agents recommended by the Fourth International Conference on the Mechanisms and Treatment of Neuropathic Pain, TCAs have greatest risk of troublesome ADRs in older adults, while the topical route of administration offers the lowest risk of ADRs and drug-drug and drug-disease interactions.

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CASE STUDIES IN THE MANAGEMENT OF NEUROPATHIC PAIN IN OLDER PATIENTS

PENNSTATE
Milton S. Hershey Medical Center
College of Medicine

Posttest

Instructions: To receive CME credit, complete the posttest and evaluation. Participants must receive a score of 80% or better to receive credit.

POSTTEST

1. Which of the following is *not* a peripheral nervous system mechanism of neuropathic pain?
   a. Collateral sprouting
   b. Masking of silent nociceptors
   c. Peripheral neuron sensitization
   d. Sympathetic postganglionic fiber invasion of dorsal root ganglia

2. Which of the following is *not* an important component of neuropathic pain assessment in older adults?
   a. Comprehensive and focused history, including outcomes of previous treatments
   b. Clinical evaluation, including assessment of somatosensory function
   c. Impact of pain on patient's quality of life and patient's therapeutic goals
   d. Quantitative thermal sensitivity testing

3. Which of the following is *not* a factor that complicates polypharmacy in older adults, often required for effective treatment of neuropathic pain?
   a. Increased risk of drug-drug interactions
   b. Increased risk of drug-disease interactions
   c. Pharmacokinetic and pharmacodynamic differences that can contribute to decreased sensitivity to adverse drug reactions
   d. Variability in symptoms and treatment response between patients with the same diagnosis

4. Which statement about topical treatments for neuropathic pain is *not true*?
   a. After application to intact skin, topical agents result in clinically significant serum drug levels.
   b. The lidocaine patch 5% is FDA approved for neuropathic pain caused by postherpetic neuralgia and is recommended as a first-line treatment.
   c. Topical formulations of capsaicin, clonidine, and EMLA have not been consistently effective for treatment of neuropathic pain in clinical trials.
   d. Topical agents possess a low risk of systemic side effects and drug interactions.

5. Which of the following is considered an advantage of using gabapentin vs other anticonvulsant agents for the treatment of neuropathic pain in older adults?
   a. Gabapentin is associated with fewer drug-drug interactions.
   b. Gabapentin has a short half-life in some older patients.
   c. Dosing reduction is not necessary in patients with renal dysfunction.
   d. It can take 4 to 7 days to achieve steady state concentrations.

6. Three anticonvulsant agents with FDA approval for treatment of neuropathic pain are:
   a. Carbamazepine, oxcarbazepine, and gabapentin
   b. Pregabalin, gabapentin, and lamotrigine
   c. Carbamazepine, gabapentin, and pregabalin
   d. Carbamazepine, gabapentin, and valproic acid

7. The first category of pharmacologic agents that proved effective for treatment of neuropathic pain was:
   a. Anticonvulsants
   b. Tricyclic antidepressants
   c. Topical anesthetics
   d. Opioids

8. Which statement about use of antidepressants for treatment of neuropathic pain is *true*?
   a. Selective serotonin reuptake inhibitors have fewer adverse effects and are generally better tolerated than tricyclic antidepressants.
   b. The adverse effect profile of selective serotonin reuptake inhibitors limits their usefulness in older adults.
   c. Tricyclic antidepressants are considered second-line agents for treatment of neuropathic pain
   d. Selective serotonin reuptake inhibitors are now considered first-line agents for treatment of neuropathic pain.

9. Which of the following is important when considering tramadol for use in treatment of neuropathic pain in older adults?
   a. Possible adverse effects, such as dizziness, somnolence, orthostatic hypotension
   b. A patient's seizure history
   c. A patient's history of substance abuse
   d. All of the above

10. Which is a *true* statement about the use of opioids in treatment of neuropathic pain?
    a. Recent studies have not shown opioids to be effective for neuropathic pain syndromes.
    b. Nausea caused by opioids has contributed to an increased incidence of falls resulting in fractures.
    c. Opioid analgesics are among the first-line agents recommended for treatment of neuropathic pain.
    d. The most common adverse effects associated with opioid use in older adults are cognitive impairment and substance abuse.

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Case Studies in the Management of Neuropathic Pain in Older Patients

Presented by

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the Office on Women's Health

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Tiagabine
Isosorbide dinitrate
Lamotrigine
Oxcarbazepine
Paroxetine
Topical cream containing amitriptyline and ketamine
Topiramate
Tricyclic antidepressants (ie, desipramine, doxepin, nortriptyline)
Valproic acid
Venlafaxine

FDA-APPROVED FOR TREATMENT OF NEUROPATHIC PAIN

Capsaicin (PHN, DPN)
Carbamazepine (TGN, PHN)
Duloxetine (DPN)
Gabapentin (PHN)
Lidocaine patch 5% (PHN)
Pregabalin (DPN, PHN)

FDA-APPROVED FOR TREATMENT OF MODERATE TO SEVERE PAIN

Opioid analgesics (ie, levorphanol, methadone, oxycodone)

Tramadol

DPN=diabetic peripheral neuropathy; PHN=postherpetic neuralgia; TGN=trigeminal neuralgia.

"Case Studies in the Management of Neuropathic Pain in Older Patients" is a self-study newsletter designed for geriatricians, neurologists, family practitioners, internists, nurse practitioners, and other healthcare professionals who treat older patients with neuropathic pain. Continuing Medical Education credit will be awarded to physicians who successfully complete this activity. Participation should take approximately 1 hour. To complete this activity and receive credit, the participant should:

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EDUCATIONAL OBJECTIVES

After reading this publication, the participant should be able to:

- Explain that neuropathic pain can arise from multiple conditions and can originate from a combination of several mechanisms.
- Identify the important components of neuropathic pain assessment in older adults.
- Describe the need for rational polypharmacy in effective management of neuropathic pain and how to minimize risk and maximize benefits when treating older patients.
- Identify first- and second-line medications for treatment of neuropathic pain and the advantages and disadvantages of each in older adults.
- Apply these assessment and treatment recommendations to effectively manage neuropathic pain in older adults.

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CASE STUDIES IN THE MANAGEMENT OF NEUROPATHIC PAIN IN OLDER PATIENTS

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