Management of Neuropathic Pain in the Geriatric Population

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KEYWORDS

• Neuropathic pain • Neuropathy • Geriatrics • Elderly • Management • Treatment

KEY POINTS

- Neuropathic pain is common and a major cause of morbidity and suffering in the geriatric population.
- It is important to differentiate neuropathic pain from other types of pain, as the treatment options are different than those used for nociceptive or visceral pain.
- Clinicians must take greater caution in treating neuropathic pain in the elderly to avoid drug-drug interactions and iatrogenic effects of medications.
- Alternative nonmedication therapies and topical treatments should be considered given the lack of systemic effects.
- When systemic medications are needed, initiate with monotherapy at lowest possible doses and titrate up slowly while monitoring closely for adverse effects.

INTRODUCTION

The International Association for the Study of Pain defines neuropathic pain as pain caused by a lesion or disease of the somatosensory nervous system.[1] Older adults are at an increased risk of neuropathic pain because many diseases that cause neuropathy increase in incidence with age. These include diabetes (diabetic neuropathy), herpes zoster (postherpetic neuralgia), spinal degenerative disease, radiculopathies, many cancers and associated chemotherapy use, stroke (central neuropathic pain), and limb amputations (phantom limb pain).[2] Other common causes of neuropathy include vitamin deficiencies, alcohol abuse, and human immunodeficiency virus (HIV).[3] There are limited

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data on the prevalence of neuropathic pain in the elderly population, although some reports indicate a prevalence of up to 32%.[4–6] Despite neuropathic pain being common and representing a major cause of morbidity and suffering in the elderly population, older adults are underrepresented in clinical trials of medications for neuropathic pain, making it difficult to generalize the benefits and risks of treatment of older individuals.[2]

CLINICAL FEATURES OF NEUROPATHIC PAIN AND DISTINGUISHING FROM OTHER TYPES OF PAIN

Neuropathic pain is characterized by several symptoms and signs. Neuropathic pain classically has a burning, electrical, or sharp quality. Unlike nociceptive pain, patients will also often have other associated "positive" symptoms such as tingling, prickling, and skin tightening sensations along with "negative" symptoms such as numbness, loss of sensation, and a "falling asleep" sensation.[7] Furthermore, patients with neuropathic pain will often have neurologic examination findings consistent with a peripheral neuropathy syndrome such as distal symmetric polyneuropathy, pure small fiber neuropathy, and compression mononeuropathy (see chapter in this issue titled, "A clinical approach to disease of peripheral nerve"). Outside of peripheral neuropathy, several other neurologic diseases are associated with neuropathic pain. These diseases include cervical and lumbar radiculopathy, herpes zoster, trigeminal neuralgia, post-stroke pain, and postspinal cord injury pain.[8]

DIAGNOSIS OF NEUROPATHIC PAIN

The clinical features of neuropathic pain and neuropathy form the groundwork for diagnosis. There are screening tools such as the Neuropathic Pain Scale and the Neuropathic Pain Questionnaire that can aid in diagnosis and quantification of severity.[9,10] These scales, however, fail to identify 10% to 20% of patients with neuropathic pain, so they are no substitute for careful clinical assessment.[11]

Although self-reporting is considered the gold standard for evaluating pain, older adults may have difficulties communicating about their pain for a variety of reasons including cognitive impairment and language dysfunction.[12] Any acute change of behavior in the elderly, especially those with difficulties communicating, should prompt providers to consider pain as a potential cause. It may be important to obtain collateral information from family members about the patient's expression of pain. There are also behavioral scales for pain evaluation in elderly patients with communication disorders such as Algoplus and Doloplus, although these were not specifically developed for neuropathic pain.[5,13–15] These observational scales, especially for patients with dementia, focus on facial expressions, body language, and vocalizations.[16] It is also important to recognize that a relationship exists between the effects of neuropathic pain on mood and sleep dysfunction.[17] A study of patients aged 65 years and older with postherpetic neuralgia found that the pain interfered most with general activity, mood, sleep, and enjoyment of life.[18] Another study in patients with painful diabetic neuropathy with a mean age of 61 years reported that more than 60% reported moderate or severe interference with general activity, mood, walking ability, normal work, sleep, and enjoyment of life.[19] The presence of mood and sleep disorders should prompt a consideration into searching for provoking causes of pain including peripheral neuropathy. There can be a relationship between conditions such as anxiety or depression and pain, and managing these psychological comorbidities is important.[20] In a study examining predictors of new-onset distal neuropathic pain in HIV-infected individuals, older age and more severe depression both conferred a significant risk.[21]

Patients with suspected neuropathic pain should also be evaluated for other associated findings of peripheral neuropathy. The evaluation of patients with suspected

peripheral neuropathy via physical examination, laboratory testing, electrodiagnostic testing, and nerve biopsy is covered in other articles in this series.

TREATMENT

Treatment of neuropathic pain focuses on identifying and treating reversible causes (if any) while simultaneously providing symptom management. It is important that clinicians and patients understand that providing disease-specific therapy does not necessarily mean resolution of symptoms. For example, this may be the case with diabetes where chronic axonal changes are slow to resolve or may even be irreversible.[22] Furthermore, most patients do not achieve complete pain relief with symptomatic treatment but can expect the pain to be more tolerable.[20] Improvement in patient's function and quality of life is paramount rather than eradication of pain, which is often not possible. For these reasons, it is important to set realistic expectations of treatment goals with patients and explain that predicting treatment response is difficult and there is sometimes a trial and error period.

Each geriatric patient must be treated individually in the context of their clinical situation, comorbidities, metabolic function, other medications, and cognitive status. Given multiple comorbidities, polypharmacy, and physiologic changes affecting drug metabolism are all common in the geriatric population, the risk of iatrogenic disease and serious drug-drug interactions are high.[5] Studies evaluating drugs for neuropathic pain are limited in the elderly population, and randomized controlled trials often exclude elderly patients.[23] It is advisable to initiate with monotherapy at the lowest possible doses with slow upward titration to analgesic effect while monitoring for adverse effects.[5,6,24] The risks and benefits of each medication must be considered in each patient, and interval monitoring for adverse reactions and efficacy should be planned.[25] **Table 1** contains a list of pharmacologic therapies in the elderly with starting doses, suggested dose increment, typical dose, and potential adverse effects. Clinicians should frequently reassess how the neuropathic pain affects the patient's quality of life, activities of daily living, and functional status.[26]

Most randomized controlled drug trials in neuropathic pain have been for limited indications. The US Food and Drug Administration (FDA) has approved 6 medications for 3 neuropathic pain syndromes: painful diabetic neuropathy (pregabalin, duloxetine, and capsaicin 8% patch), postherpetic neuralgia (gabapentin, pregabalin, 5% lidocaine patch, capsaicin cream, and capsaicin 8% patch), and trigeminal neuralgia (carbamazepine).[20] Non-FDA approved medications have also been found to be effective in clinical practice.[27] The current National Institute for Health and Care Excellence guidance for the pharmaceutical management of neuropathic pain suggests offering a choice of amitriptyline, duloxetine, gabapentin, or pregabalin as initial treatment of neuropathic pain (with the exception of trigeminal neuralgia) and switching if the first, second, or third drugs are not effective or tolerated.[28] This concurs with other recent guidelines from the Neuropathic Pain Special Interest Group (NeuPSIG) of the International Association for the Study of Pain, which has gabapentin, pregabalin, serotonin-norepinephrine reuptake inhibitors (SNRIs; duloxetine/venlafaxine), and tricyclic antidepressants (TCAs) as first-line agents and capsaicin 8% patches, lidocaine patches, and tramadol as second-line agents.[27] In frail and elderly patients, lidocaine patches may be considered as a first-line agent.[27]

PHARMACOLOGIC OPTIONS

Calcium Channel α2-δ Ligands (Gabapentin/Pregabalin)

Gabapentinoids are a first-line class of medications in the treatment of neuropathic pain.[11,29,30] They bind to the voltage-gated calcium channels at the α2-δ subunit

Table 1
Pharmacologic therapies for neuropathic pain in the elderly

Drug Class	Agent	Route	Initial Dose	Dose Increment	Typical Dose	Adverse Effects
Calcium Channel α2-δ Ligands	Gabapentin	PO	100–300 mg daily three times/d	100-300mg daily in 1-3 divided doses	300-2700mg daily in 1-3 divided doses	• Sedation, altered mental status • Dizziness, ataxia • Visual disturbances • Peripheral edema; recommend caution with heart failure • Administer at lower doses in renal failure to avoid excess sedation, dizziness
	Pregabalin	PO	25–75 mg daily three times/d	25-75mg daily in 1-3 divided doses	50-300mg daily in 2-3 divided doses	
Serotonin-Norepinephrine Reuptake Inhibitors	Duloxetine	PO	20–30 mg daily	Increase 20–30 mg every 1 wk	60 mg daily	• Sedation • Nausea, constipation • Dry mouth • Hypertension, palpitations • Caution with cardiac conduction derangements • Taper on cessation to avoid withdrawal syndrome
	Venlafaxine	PO	37.5 mg daily	37.5–75 mg every 1-2 wk	150–225 mg daily (extended release)	

Tricyclic Antidepressants	Amitriptyline Desipramine Nortriptyline	PO	10–20 mg daily	Increase 10–25 mg every 1 wk	25–75 mg daily	• Fewer anticholinergic effects with nortriptyline: sedation, dizziness, falls, dry mouth, constipation, urinary retention • Caution with cardiovascular disease and cardiac conduction derangements • Avoid in glaucoma, prostate hypertrophy, angina, heart failure, cardiac conduction abnormalities
Alpha Lipoic Acid		IV/PO	600 mg		600–1800 mg daily	• Nausea and vomiting
Cannabinoids		INH/PO				• Sedation • Dizziness • Confusion/psychosis • Abuse potential
Sodium Channel Antagonists	Carbamazepine	PO	100–200 mg daily	100-200mg/day every 1 wk	600-800mg/day in 3-4 divided doses	• Sedation • Dizziness • Skin rash • Rarely, can cause hyponatremia, leukopenia, thrombocytopenia, and liver damage

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Table 1
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Drug Class	Agent	Route	Initial Dose	Dose Increment	Typical Dose	Adverse Effects
Topical Agents	Lidocaine patch 4 or 5% Capsaicin patch/cream	Topical Topical	1–4 patches daily for maximum 12 h 0.075% (low-dose cream)/8% (high-dose patch)			• Local skin irritation, redness, rash • Erythema, burning, and pain at application site • Consider topical pretreatment with lidocaine and oral analgesics before application

and produce changes in neurotransmitter release.[31] They have an overall better safety profile than many other oral therapeutic options, with few drug-drug interactions due to their lack of metabolism or effect on hepatic enzymes. However, they can cause adverse effects such as sedation, dizziness, ataxia, visual disturbances, altered mental status, or peripheral edema.[32] Patients with chronic kidney disease and especially those on hemodialysis are more susceptible to complications due to reduced clearance of these agents, as they depend on renal excretion for elimination.[33] Clinical guidelines recommend conservative dosing of gabapentin and pregabalin, up to a maximum dose of 300 mg or 100 mg daily, respectively, for treatment of neuropathic pain in those with end-stage renal disease.[33]

A Cochrane review found moderate-quality evidence that oral gabapentin has an important effect on pain in some people with moderate or severe neuropathic pain after shingles or due to diabetes.[34] Typical starting dose of gabapentin is 100 to 300 mg three times a day with titration every 1 to 7 days by 100 to 300 mg/d as tolerated up to a maximum dose of 3600 mg/d[20] To reduce daytime side effects including sedation, providers may start with a single bedtime dose; this may also be a favorable strategy when the pain is most bothersome at night. There may be a delayed onset to reach analgesic effect, taking up to 2 months.[8] Elderly patients should be started on the lowest dose (100 mg at bedtime) and titrated up slowly assessing for adverse effects.[25]

A Cochrane review found moderate-quality evidence that oral pregabalin has an important effect on pain in some people with moderate or severe neuropathic pain after shingles or due to diabetes.[35] Pregabalin doses start at 150 mg/d divided in 2 to 3 doses with titration every 1 to 2 weeks to a maximum dose of 300 mg/d[8] However, older adults should be started at low doses (50 mg at bedtime) and titrated up slowly to assess tolerance.[25] It should be used cautiously in patients with heart failure, because cases of decompensated heart failure with pregabalin use have been reported.[3]

Serotonin-Norepinephrine Reuptake Inhibitors

SNRIs, such as duloxetine and venlafaxine, regulate descending inhibitory pathways of pain via inhibition of serotonin and norepinephrine reuptake. SNRIs can also be used for treatment of comorbid depression and anxiety.[36] SNRIs have a better safety profile than TCAs, but there are still many potential adverse effects in the elderly including nausea, constipation, hot flashes, hyperhidrosis, palpitations, dry mouth, hypertension, and drug-drug interactions including a risk of serotonergic syndrome.

Duloxetine is considered a first-line neuropathic agent.[11,27,28] Duloxetine has a single daily dosing regimen and also acts as an antidepressant. It has been found to be effective in maintaining pain relief for 6 months in an open-label trial in patients with painful diabetic neuropathy.[37] Older adults should be started at 20 to 30 mg once daily and after 1 week can be increased to 60 mg once daily as tolerated.[23,25]

Venlafaxine is used in the treatment of major depressive disorder and generalized anxiety disorder, social anxiety disorder, panic disorder, and agoraphobia. A Cochrane review evaluating venlafaxine in neuropathic pain found that there is an inadequate amount of information available to promote it as a first-line agent for neuropathic pain but that it is a reasonably well-tolerated drug and may be of some benefit in patients not able to tolerate other drugs.[38] If it is to be started, it should be at a low dose of 37.5 mg daily and blood pressure and heart rate should be monitored.[25] It should not be abruptly stopped, as there can be a withdrawal syndrome.[20]

Tricyclic Antidepressants

TCAs, such as amitriptyline, are often considered first-line medications for treating neuropathic pain. They work by inhibiting the reuptake of serotonin and

norepinephrine and blocking ion channels, which reinforces the descending inhibitory pain pathways.[36,39] They should, however, be used with significant caution in the geriatric population. The anticholinergic adverse effects may be significant in elderly patients and can provoke dizziness, sedation, orthostatic hypotension, dry mouth, and constipation. They are contraindicated in patients with glaucoma, prostate hypertrophy, or certain cardiac conditions including unstable angina, recent myocardial infarction, heart failure, and abnormal cardiac conduction. They can also contribute to cognitive disorders or confusion. Because of this risk profile, other neuropathic agents may be preferable in the geriatric population.[40] Tertiary amine TCAs such as amitriptyline, imipramine, and clomipramine are not recommended at doses greater than 75 mg/d in older adults because of major anticholinergic and sedative side effects and potential risk of falls.[27] Nortriptyline is a secondary amine TCA that has fewer anticholinergic side effects, but a Cochrane review found little evidence to support the use of nortriptyline to treat neuropathic pain.[41]

Carbamazepine

Carbamazepine is approved by the FDA for treatment of trigeminal neuralgia, which is a specific form of neuropathic pain that is not fully covered in this article but deserves mention. A Cochrane review in 2014 found that it is also probably effective in some people with chronic neuropathic pain but with reservations given the lack of trial evidence.[42] The drug is a sodium channel antagonist and works by slowing the recovery rate of the voltage-gated sodium channels.[8] The precise mechanism of action in relation to relief of neuropathic pain remains uncertain, but they reduce the ability of the neuron to fire at high frequency and likely inhibits ectopic discharges.[42,43] Side effects include drowsiness, difficulties with balance, skin rash, and dizziness. Rarer severe side effects include agranulocytosis, thrombocytopenia, and liver damage. Regular monitoring with complete blood count and liver function testing is recommended. There is a high potential for drug-drug interactions, as carbamazepine is an inducer of the hepatic P450 cytochrome system. It also has a narrow therapeutic window.[44] Dosing guidelines suggest starting at 200 to 400 mg/d in 2 to 4 divided doses per day depending on preparation and gradually increasing over several weeks in increments of 100 to 200 mg every 2 days as needed. The usual maintenance dose is 600 to 800 mg/d with a maximum dose of 1,200 mg/d. In chronic therapy, it should be withdrawn gradually over 2 to 6 months to minimize withdrawal symptoms.[45] Therapeutic drug monitoring may be useful, especially within the first few months of therapy, as carbamazepine induces hepatic enzymes, thereby increasing its own metabolism. It should be used with caution in the elderly population, especially given the significant drug interactions and the need for laboratory monitoring with its use.

Opioids

Opioids are considered second- or third-line agents in the treatment of neuropathic pain. Systematic review and meta-analyses find opioids do provide analgesic effect in neuropathic pain in the short term (the average duration of treatment in trials was 5 weeks with a range of 1–16 weeks), although little is known about long-term efficacy.[27,46] There are significant safety concerns including opioid abuse and addiction in patients suffering from chronic pain. Every patient should be assessed for risk factors related to potential abuse and strictly monitored. The lowest effective dose should be prescribed. Opioids should only be used in certain situations with severe, refractory pain such as during titration of a first-line medication, acute exacerbations of chronic neuropathic pain, or in the setting of malignancy.[8]

Constipation, somnolence, delirium, dizziness, nausea, and dry mouth are the most commonly reported adverse effects of opioids.[47] Respiratory depression is one of the major concerns of opioid therapy, especially in patients also using benzodiazepines or barbiturates.[48] Patients generally develop tolerance to all of the adverse effects except constipation, and it is important that a bowel regimen is started with initiation of opioids.

Tramadol is a weak opioid that acts as both mu-opioid agonist and norepinephrine and serotonin reuptake inhibitor. It has a similar side effect profile to other opioids. It also lowers the seizure threshold and can cause serotonin syndrome if combined with other selective serotonin reuptake inhibitors. Doses should be reduced in elderly patients and in those with renal or hepatic impairment.[49] A Cochrane review found only low- or very low–quality evidence and was unable to make a conclusion about its efficacy and safety in treating neuropathic pain.[49,50]

Strong opioids include morphine, hydromorphone, oxycodone, and fentanyl. Caution should be used in the elderly given the increased half-life of the active drug metabolites and especially if there is hepatic or renal failure.[27] When considering use of opioids to control neuropathic pain, it may be most appropriate to refer to a pain management specialist.

Alpha Lipoic Acid

Alpha lipoic acid (ALA) is an antioxidant substance that has been studied in the treatment of neuropathic pain, specifically in diabetic peripheral neuropathy (DPN). It is thought to relieve pain by reducing oxidative stress, which is an important mechanism in the pathogenesis of diabetic peripheral neuropathy.[49] Based on a 2012 meta-analysis, ALA, 600 mg, administered intravenously daily for 3 weeks led to a clinically significant reduction in neuropathic pain in the short term.[51] A randomized, double-blind, placebo-controlled trial demonstrated oral treatment with ALA, 600 mg, daily for 5 weeks improved neuropathic symptoms in those with distal symmetric polyneuropathy, and a prospective, double-blinded, placebo-controlled study demonstrated oral 600 mg ALA twice daily for DPN over 6 months is effective, safe, and tolerable.[52,53] There is currently a Cochrane review pending to assess the effects of ALA as a disease-modifying agent in DPN.[54] Relative to other treatments for peripheral neuropathy, there are fewer side effects, although it can cause nausea and vomiting.[49]

Topical Treatments

Topical medications with their limited systemic effects warrant special consideration in the elderly population who often have multiple comorbidities and polypharmacy. They are especially useful in localized neuropathic pain where the area of maximum pain is consistent and circumscribed. A review article evaluated topical treatment of localized neuropathic pain in the elderly, including 18 randomized controlled trials. It determined that in older adults, lidocaine 5% and capsaicin 8% are effective for localized neuropathic pain and considered first-line drugs in older adults, especially in patients with comorbidities and polypharmacy.[55,56]

Lidocaine is a local anesthetic available in plaster (patch), spray, or cream that acts as a sodium-channel antagonist, and acts to reduce ectopic discharges mediating nociception.[36,55] The 4% lidocaine patch is sold over-the-counter, whereas the 5% patch requires a prescription in the United States. Both strengths of patches have the same administration guidelines and can be self-applied facilitating patient adherence.[55] Side effects are rare and are largely related to local skin reactions. Clinical experience and individual studies indicate it is effective for pain relief in older persons, although the Cochrane review in adults found no evidence from good-quality randomized controlled trials to support its use.[57] Topical lidocaine can also be used in combination with an oral

neuropathic pain medication. One study found combination of lidocaine 5% medicated plaster with pregabalin provided additional relief from pain due to postherpetic neuralgia and diabetic polyneuropathy and was safe and well tolerated.[58] The American Geriatrics Society states that all patients with localized neuropathic pain are candidates for topical lidocaine (moderate quality of evidence, strong recommendation).[25]

Capsaicin is the active ingredient of chili peppers. It binds to nociceptors in the skin, specifically the transient receptor potential vanilloid 1 receptor. Following continued capsaicin exposure, there is reversible degeneration of the nerve terminals preventing pain transmission and resulting in a reduced pain response.[8,55] A Cochrane review found there is moderate-quality evidence that high-concentration (8%) capsaicin patches can give moderate pain relief or better to a minority of people with postherpetic neuralgia and very low–quality evidence that it benefits those with HIV neuropathy and diabetic neuropathy.[59] One study found that the capsaicin 8% patch is noninferior to an optimized dose of pregabalin in relieving pain in patients with peripheral neuropathic pain with a more rapid onset of action, fewer systemic side effects, and greater treatment satisfaction.[60] Another randomized, double-blind, placebo-controlled study found that one 30-minute treatment with the capsaicin 8% patch provided modest improvements in pain and sleep quality in patients with painful diabetic peripheral neuropathy.[61] The high-concentration patch is applied by a physician for 30 to 60 minutes and may provide relief for up to 12 weeks.[55] It may require pretreatment with topical lidocaine or oral analgesia due to the intense pain with initial application, with some patients even experiencing an increase in blood pressure during the painful application. Some adverse effects include local erythema, edema, and swelling and sensory complaints of burning or stinging pain. It can cause mucous membrane irritation and must be handled by the provider and patient with caution.[8] In spite of these adverse effects, a double-blind study in patients with diabetes found the treatment to be well tolerated with no discontinuations due to drug-related reactions.[61]

ALTERNATIVE TREATMENTS

Movement and Physical Therapy

Physical therapy can help improve functionality and mobility, which is important, as neuropathy often leads to a decrease in physical activity. A focus on strengthening muscles and improving balance are crucial to successful physical therapy for neuropathy.[8] The effects of exercise may even reduce inflammation. Studies have demonstrated improvement in cutaneous nerve regeneration capacity in patients with metabolic syndrome and diabetes who undergo exercise regimens, specifically moderate intensity aerobic exercise for 150 minutes a week.[62,63] In patients with diabetic neuropathy, physical movement helps improve glycemic control, which can prevent worsening of the neuropathy.[64]

Tai chi and yoga are other types of physical engagement that have proved beneficial in ameliorating various chronic pain conditions. Tai chi is a traditional Chinese martial art consisting of low-impact, low-velocity smooth movements to improve balance, prevent falls, enhance cardiovascular health, and reduce stress. Twelve weeks of Tai chi (1 hour, 3 times per week) improved fasting blood glucose, insulin resistance, hemoglobin A1c, balance, and Total Symptom Score in diabetic neuropathy in 2 controlled trials.[65,66] Yoga has been shown to be beneficial in neurologic disorders, pain, and diabetes in multiple studies, but randomized controlled trials in neuropathy are limited.[67,68] A randomized controlled trial showed superiority of the practice of yoga postures compared with splinting in treatment of carpal tunnel syndrome for improvement in pain and grip strength.[69]

Psychotherapy

Cognitive behavioral therapy (CBT) aids patients in changing maladaptive behaviors, thoughts, and emotions by teaching coping skills and conscious confrontation of deleterious thoughts and behaviors.[64] CBT has been shown to provide benefit in patients with HIV-related peripheral neuropathy, improving pain and reducing pain-related interference with functioning in these patients.[70] A Cochrane review found insufficient evidence of the efficacy of psychological interventions for neuropathic pain given the lack of studies specifically examining this.[71] However, a study of 442 patients with chronic pain comparing the use of telephone CBT, exercise, or a combination of both showed significantly better outcomes for the combined intervention group at 6 and 9 months.[72]

There are a few studies demonstrating a benefit of other integrative psychotherapies in reducing pain and improving quality of life. Specifically, self-hypnosis was found to be useful and well tolerated in a small group of patients with HIV-related distal sensory polyneuropathy.[73] Mindfulness meditation and progressive relaxation meditation were found to be beneficial as part of a comprehensive pain management plan for older adults with painful diabetic neuropathy in 2 small studies.[74,75] However, other studies have not shown a statistically significant change on pain and quality of life with meditation in patients with neuropathic pain.[76,77]

Acupuncture

Acupuncture involves stimulation of anatomic points through solid metallic needle penetration and manipulation. It is a therapy based on traditional Chinese medicine. A systematic review and meta-analysis of acupuncture for the treatment of peripheral neuropathy showed benefit for acupuncture over control in the treatment of diabetic neuropathy and probable benefit for treatment of HIV-related neuropathy. The study concluded that more rigorously designed studies are needed using sham acupuncture.[78] However, a Cochrane review found insufficient evidence to support or refuse the use of acupuncture in treating neuropathic pain, given the studies were small and of low-quality evidence with limited generalizability.[79]

Cannabinoids

The role of cannabis-based medicines in treating neuropathic pain is controversial. A Cochrane review demonstrated a lack of high-quality evidence that any cannabis-derived product works for chronic neuropathic pain but that the potential benefits of cannabis-based medicine in chronic neuropathic pain might be outweighed by their potential harms.[80] A randomized, double-blind, placebo-controlled crossover study done in 16 patients with painful diabetic peripheral neuropathy assessing the short-term efficacy and tolerability of inhaled cannabis demonstrated a dose-dependent reduction in diabetic peripheral neuropathic pain.[81] Possible side effects include sedation, dizziness, and confusion, and its use is limited by availability, abuse potential, and the risk of precipitating psychosis.[8] Cannabinoids have a weak recommendation against their use in neuropathic pain by the NeuPSIG based on their systematic review.[27]

SUMMARY

Neuropathic pain can be challenging to diagnose and treat, especially in elderly patients. It is important to correctly diagnose neuropathic pain and evaluate possible causes, of which there are many. Pharmacologic treatments should be prescribed cautiously given the increased risk of side effects in the geriatric population. However,

it is important to not let caution impede adequate pain control. For localized pain, topical treatments should be considered. Nonpharmacologic alternative treatments should be considered as additive therapy. Frequent reevaluation to assess for analgesic effect and potential adverse events is important.

CLINICS CARE POINTS

- Neuropathic pain is common and a major cause of morbidity and suffering in the geriatric population.
- Neuropathic pain can be difficult to distinguish from other types of pain, and diagnosis requires a thorough history and physical examination.
- Referral to a neurologist and nerve conduction studies and electromyography may be required.
- Once diagnosed, further workup is required to elucidate the cause, including potential reversible causes of neuropathy.
- Symptoms of neuropathic pain can be "positive" such as burning or tingling or "negative" such as numbness.
- Pharmacologic treatments can often improve the "positive" symptoms, but it is difficult to treat the "negative" symptoms.
- It is important to differentiate neuropathic pain from other types of pain, as the treatment options are quite different than those used for nociceptive or visceral pain.
- Older adults are underrepresented in clinical trials of medications for neuropathic pain, making it difficult to generalize the benefits and risks of treatment in older individuals.
- Clinicians must take greater caution in treating neuropathic pain in the elderly to avoid drug-drug interactions and iatrogenic effects of medications.
- Alternative nonmedication therapies and topical treatments should be considered.
- When systemic medications are needed, initiate with monotherapy at lowest possible doses and titrate up slowly while monitoring closely for adverse effects.
- It is important to not be overcautious at the risk of undertreating patients' pain. Risks and benefits must be considered and frequent reevaluation is necessary.

DISCLOSURE

The authors have nothing to disclose.

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