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Managing herpes zoster in older adults: Prescribing considerations

Abstract: *NPs must be aware of special prescribing considerations for medication safety when managing the care of older adults with herpes zoster. Age-related physiologic changes of the body impact the pharmacokinetics and pharmacodynamics of antiviral and pain medications and can lead to potential adverse events.*

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Herpes zoster (HZ), commonly known as shingles, negatively impacts older adults' activities of daily living mainly due to the high level of pain and discomfort it causes. The associated acute pain and postherpetic neuralgia (PHN) diminish physical functioning, interfere with sleep, lower energy, and impair mental health.[1] Moreover, HZ impacts quality of life for many older adults who already live with the following chronic conditions: arthritis, depression, diabetes mellitus, heart disease, chronic kidney disease, asthma, chronic obstructive pulmonary disease, and neurologic disorders.[1,2]

NPs must be aware of special considerations for medication safety when managing the care of older adults with HZ. Age-related changes of the body, such as decreased kidney function and creatinine clearance (CrCl), can impact the pharmacokinetics and pharmacodynamics of antiviral and pain medications, which can lead to potential adverse events.[3]

Older adults generally live with one or more chronic conditions and are prescribed multiple medications, both prescription and over the counter (OTC). Thirty-nine percent of adults age 65 and older take five or more prescription medications, and up to 90% take OTC drugs.[4] Polypharmacy, defined as taking more than five medications concurrently, increases the risk of drug interactions and is therefore a concern for medication safety.[3,4] Additional medications, such as those for HZ management, may be the "tipping point" that results in hospitalization.[5]

Case study

Ms. C, 80, presented to the ED for altered mental status. A physical exam revealed zoster lesions on the right side of her face; there was no ocular involvement. Ms. C's medical history included rheumatoid arthritis, hypertension, hyperlipidemia, depression with anxiety, hypothyroidism, and atrial fibrillation. She had a history of recurrent HZ and PHN, which began in 2006, as well as a history of frequent falls with injuries in the past 5 years, such as fractures of the clavicle and both hips. Ms. C lives alone in a retirement apartment complex. Her son, who lives 10 miles away, has durable power of attorney for medical decisions and checks on his mother daily.

Ms. C was taking leflunomide and prednisone for rheumatoid arthritis; amlodipine and metoprolol for hypertension; levothyroxine for hypothyroidism; apixaban for atrial fibrillation; venlafaxine and desipramine for depression; buspirone for anxiety; pregabalin and lidocaine patch for PHN; polyethylene glycol 3350 for constipation; omeprazole

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for gastric ulcer prophylaxis prevention; vitamin D and calcium for vitamin D deficiency and osteoporosis; and hydrocodone/acetaminophen for pain. She was admitted to the hospital with a diagnosis of dehydration, urinary tract infection (UTI), hyponatremia, and HZ.

Initially, Ms. C's HZ treatment was I.V. acyclovir for 4 days, which was switched to oral valacyclovir, 500 mg twice daily (adjusted dose due to her low CrCl of 28 mL/min), at discharge to complete a total course of 7 days of antiviral therapy. Leflunomide was held until the HZ resolved. Hydrocodone and acetaminophen orally every 4 hours as needed and lidocaine patch 5% every 12 hours were prescribed for pain. Ms. C's UTI and hyponatremia were treated and her medical condition stabilized within 4 days. She was discharged home on 16 medications with referral for home healthcare. Ms. C has a follow-up appointment with her primary care NP in 1 week.

Antiviral medications for HZ

The antiviral medications acyclovir, famciclovir, and valacyclovir are prescribed for treatment of the acute phase of HZ (as soon as possible or within 72 hours of the lesions' appearance) to resolve the lesions and decrease the acute pain severity.[6] Antivirals will not prevent PHN, although some evidence has shown that they are effective in decreasing PHN duration.[7] These antivirals are classified as nucleoside analogues, which block the virus's DNA synthesis, thus blocking viral cell replication.[6]

Oral famciclovir and valacyclovir are better absorbed than oral acyclovir, resulting in higher antiviral activity.[6]

The primary goal of treatment for patients with HZ or PHN is to control their pain and restore their function and quality of life.

Famciclovir (every 8 hours for 7 days) and valacyclovir (three times per day for 7 days) also have lower dosing frequency than oral acyclovir (five times per day for 7 days) but are more expensive. Antiviral medication adverse reactions include nausea, vomiting, headache, central nervous system (CNS) disturbances, and dizziness.[8] Medication selection and treatment adherence are important considerations, especially for older adults who live alone and have frailty or comorbidities such as depression or cognitive impairment.

Antiviral medications are excreted through the kidneys.[8] With aging, there is generally a decline in kidney mass and function leading to a decrease in CrCl and the kidney's ability to excrete medications (this decline may vary considerably by individual). Assessing the patient's kidney function by calculating the estimated CrCl is essential. An easy formula to use is the Cockcroft and Gault formula:

Estimated CrCl = [[140–age (year)] × weight (kg)] / [72 x serum Cr (mg/dL)](multiply by 0.85 for women).[9,10]

Electronic references, such as UpToDate, Epocrates, and GlobalRPh, provide CrCl calculators.[11-13] NPs should not rely on blood urea nitrogen level, which is affected by muscle mass, hydration level, anemia, and dietary protein intake.[9,11] Prescribing lower doses of antiviral medications for patients with kidney impairment (based on CrCl) and educating patients regarding the importance of staying hydrated are beneficial.[8,11,14] Antiviral medications should be scheduled after a patient receives dialysis treatment.[8]

Pain medications

The primary goal of treatment for patients with HZ or PHN is to control their pain and restore their function and quality of life.[15-18] Pain medications for HZ or PHN include analgesics, opioids, antiepileptic adjuvant analgesics, and tricyclic antidepressants (see *Prescribing considerations and patient education for HZ and PHN*).[14,17,18]

Analgesics such as nonsteroidal anti-inflammatory drugs (NSAIDs) and acetaminophen are useful for mild pain, either alone or in combination with an opioid analgesic, such as hydrocodone.[19] NSAIDs are associated with increased risk of adverse cardiovascular thrombotic events, including myocardial infarction (MI) and stroke, heart failure, and worsening hypertension.[20] NSAIDs can also decrease renal blood flow and impair kidney function.[14,15] There is also a potential risk for gastrointestinal (GI) ulcerations with chronic use of NSAIDs.[20]

Patients with a history of GI bleeding or ulcerations will benefit from a proton pump inhibitor, although the effectiveness is inconclusive.[20] Lidocaine 5% patch may be a better alternative because it has few adverse reactions and can be used as an adjunct pain medication applied to intact skin for PHN.[14,17]

For moderate-to-severe pain that disturbs sleep, stronger opioid analgesics may be needed (such as oxycodone or morphine) but for a short period. Physical changes caused by aging affect the number and sensitivity of drug receptors and may increase a drug's therapeutic effects and increase its adverse reactions.[19] Two major adverse reactions that are particularly concerning for older adults include drowsiness and constipation.[21]

Drowsiness increases the risk of falls. Patients with impaired alertness due to drowsiness may accidently take

Prescribing considerations and patient education for HZ and PHN[8,11,16,18]

Medication	Special considerations for older adults	Patient education
Antivirals: • Acyclovir • Famciclovir • Valacyclovir	• Monitor serum creatinine and CrCl levels. Adjust dose if indicated. • Monitor medication adherence. • Check for possible medication interactions.	• Drink plenty of fluids. • Report decreased urine output. • Avoid alcohol. • Use visual cues at home as a reminder to take medication. • Report any unusual symptoms. • Do not get the shingles vaccine while on these medications.
NSAID analgesics	• Increase risk for GI bleeding. • Consider gastroprotective agents. • Do not use in patients with heart failure. • Monitor kidney function.	• NSAIDs are not for prolonged use; take with food or milk to protect stomach/prevent ulcers or bleeding.
Topical analgesics for PHN: • Lidocaine patch • Topical capsaicin	• Do not apply capsaicin near eyes or mucous membranes. • Observe for skin irritation.	• Take previous lidocaine patch off before putting a new patch on. Apply only to intact skin. • Do not apply on open lesions or irritated skin. • Stop and report to NP if skin irritation develops where medication is applied. • Wash hands after applying capsaicin. • Avoid getting medicine near eyes or mucous membranes.
Opioid analgesics:* • Opioid-acetaminophen combinations	• Opioids are sedating and increase the risk of delirium and falls. • Assess for fall risk. • Prescribe medication for constipation while on opioids. • Limit acetaminophen from all sources (including OTC) to 3 g/day.	• Adverse reactions include respiratory depression, dizziness, sedation, constipation, and urinary retention. • Avoid alcohol, which increases sedating effects. • Do not operate machinery while taking opioids.
Antiepileptic adjuvant analgesics for PHN: • Pregabalin • Gabapentin	• Dose adjustments are needed for patients with kidney impairment. • Monitor CrCl and kidney function. • Monitor platelet levels. • Monitor fall risk.	• Do not abruptly stop taking drugs; contact the NP. • Adverse reactions include dizziness, somnolence, blurred vision, increased risk for falls, and peripheral edema.

*Medications listed are potentially inappropriate for use in older adults.

the wrong medication or too much medication. Opioid-induced constipation is especially problematic for older adults because of the decreased GI motility from aging and should be proactively managed.[21]

Patients unresponsive to treatment with opioid agents may benefit from a different medication regimen of nonopioid adjuvant medications that are more specific to the treatment of neuropathic pain, such as the antiepileptic medications gabapentin or pregabalin, which are FDA approved for PHN.[22] However, these medications have increased permeability of the blood-brain barrier, which can result in CNS adverse reactions such as somnolence.[23] Both gabapentin and pregabalin are excreted by the kidneys; therefore, doses should be adjusted accordingly to the patient's estimated CrCl.[8]

Tricyclic antidepressants such as nortriptyline or amitriptyline are used off-label for the treatment of neuropathic pain; however, they should be used with caution or avoided in older adults because of the pharmacokinetic and pharmacodynamic adverse reactions. Adverse reactions from tricyclic antidepressants include increased risk of falls from sedation and orthostatic hypotension, and adverse cardiovascular events including MI, stroke, and atrioventricular block.[14] These drugs are contraindicated in patients during the acute recovery phase following an MI.[14] Nortriptyline is also associated with Brugada

syndrome.[14] Tricyclic antidepressants are not as well tolerated in older adults because of their anticholinergic effects.[14]

Patients who require complex drug combinations or invasive treatments should be referred to a pain management center.

Older adults are more sensitive to drugs with anticholinergic effects, which can lead to imbalance, disorientation, urinary retention, and decreased GI peristalsis. Tricyclic antidepressant medications are listed on the Beers Criteria for Potentially Inappropriate Medication Use in Older Adults.[19] The Beers Criteria is an invaluable evidence-based resource that aids clinical decision-making and helps NPs prescribe medications safely. The caveat is that this criteria list should not supersede clinical judgment or a patient's need for pain management (see *Additional prescribing resources*).[19]

Some older adults with PHN will not reach adequate pain control with any of the frontline medications. For these patients, other pharmacologic and nonpharmacologic treatments may be necessary. Patients who require complex drug combinations or invasive treatments should be referred to a pain management center.[23]

Key points

NPs should consider the physiologic aging changes and the patient's comorbidities when prescribing medications for HZ and PHN for older adults. The best prescribing management is to begin with a medication that has few adverse reactions and a desirable effect on pain. The general principle is to start with a low dose and slowly titrate as tolerated until pain is ameliorated to a desirable level.[3] If titrated too quickly, adverse reactions such as drowsiness, confusion, incontinence, impaired balance, or falls will likely result.[3,15] A prudent approach is to assess how the patient has tolerated pain medications in the past.

Another key point is that no one treatment option will work for all patients. Oftentimes, combinations of medications must be trialed to achieve a tolerable balance of pain control and adverse reactions.[15] Pain control may mean the pain is ameliorated but not necessarily resolved. Therefore, it is important for NPs to set realistic goals and communicate frequently in order for their patients to know the pain medications' effectiveness and tolerability.[3]

Additional prescribing resources

American Chronic Pain Association Resource Guide to Chronic Pain Treatment
www.theacpa.org/uploads/documents/ACPA_Resource_Guide_2016.pdf

Beers Criteria for Potentially Inappropriate Medication Use in Older Adults
http://geriatricscareonline.org/ProductAbstract/american-geriatrics-society-updated-beers-criteria-for-potentially-inappropriate-medication-use-in-older-adults/CL001

Monthly Prescribing Reference
www.eMPR.com

UpToDate
www.uptodate.com

Prescribing priorities

Prescribing considerations for the case study patient should include identifying risk factors such as age, comorbidities, being immunocompromised due to medications for rheumatoid arthritis, polypharmacy (including multiple pain medications), and a history of falls. At the patient's follow-up appointment, the NP's assessment should confirm that the zoster lesions are resolving. If the lesions have extended close to the eyes, a referral to an ophthalmologist is necessary. The NP should also evaluate if the patient completed and tolerated the antiviral medications prescribed at hospital discharge. The patient's mental alertness should be reassessed, as confusion, drowsiness, and somnolence are possible adverse reactions of the pain medications. Follow-up lab work should include CrCl.

The second priority is to evaluate the pain management: How is the pain affecting the patient's self-care? How is the patient managing at home? Is the pain medication effective? NPs should also inquire about how the patient is tolerating adverse reactions, including constipation. This case study patient has a history of falls, so it is important to also determine if she experienced any dizziness or falls since discharge. Furthermore, it is important to collaborate and communicate with the home health nurse to continue the patient's pain management evaluation.

The third priority is to conduct medication reconciliation. The case study patient was discharged from the hospital with 16 medications, which is alarming. It is critical to review medications (including OTC) with the patient. It is important to assess patients' understanding of the prescribed medications and ask how they track medications at home. NPs may consult with the pharmacist regarding polypharmacy and drug interactions. It is also important to

communicate with the patient's medical specialists regarding any medication changes or concerns.

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