Battling shingles: Fine-tune your care

Which of the 3 antiviral agents works best for accelerating rash healing and reducing pain? And what about corticosteroids—are they a good idea, or not? Read on.

CASE

Jane T, a 53-year-old patient, calls her family physician’s office for a same-day appointment; she has severe right upper quadrant pain that developed a few hours ago. When Jane comes in, she tells her physician that the pain feels like the gallbladder attacks she used to have—before her gallbladder was removed 2 years ago. She has nausea but no vomiting, is afebrile, and has no urinary symptoms.

A series of in-office tests—urinalysis, complete blood count, comprehensive metabolic profile, amylase, and lipase—are all normal. The physician gives Jane an intramuscular injection of ketorolac and a prescription for oral tramadol, and sends her for a right upper quadrant ultrasound, which is also normal. The next morning, the pain intensifies, and Jane goes to the emergency department, where she undergoes computed tomography of the abdomen and pelvis—also normal. After a night in the hospital for observation, she is released.

She returns to the family physician 3 days later, this time with an erythematous papular rash in a dermatomal distribution over her back and right upper quadrant that her doctor immediately recognizes as shingles.

Jane is not alone. Each year, about 1 million US residents develop herpes zoster (HZ), and 70% to 80% of them experience prodromal pain in the affected dermatome. For some, the pain is significant enough to prompt a medical work-up to rule out other potential causes, such as myocardial infarction, nephrolithiasis, pancreatitis, cholecystitis, and appendicitis.

The time and resources spent on such a work-up may be unavoidable when a patient presents with severe pain. But alert primary care physicians can avoid unnecessary diagnostic tests by being aware of the prodromal symptoms of HZ and being on the lookout for the rash that follows.

Age alone is a key factor in the detection of HZ, of course. One in 3 people will develop shingles during their lifetime.
with half of all cases occurring in people ages 60 and older. In addition to early detection and treatment, physicians can do their part to battle HZ by routinely recommending the shingles vaccine (Zostavax) to patients in this age group.

Diagnosing HZ: From prodrome to rash
For many patients, an abnormal skin sensation on one side of the body, such as itching, burning, or altered sensitivity to touch, is the first symptom of HZ. These sensations, including pain that can range from mild to severe, may precede the rash by days or even weeks. Systemic symptoms are far less common; less than 20% of patients develop fever, headache, malaise, or fatigue as part of the HZ prodrome. The shingles rash is usually unilateral and does not cross the midline. However, it may occur in up to 3 adjacent dermatomes. The trunk is the most common site for the rash, but it may also develop on the face, buttocks, or other parts of the body. The lesions start as erythematous papules and evolve into vesicles within 12 to 24 hours.

Once the rash emerges, HZ can usually be diagnosed clinically in a primary care setting, and laboratory testing should be considered only when diagnosis is uncertain. In a cohort study of 260 patients older than 50 years with clinically diagnosed HZ, varicella zoster IgA or IgM was positive in 61% of patients at the time of presentation, and in 91% of patients 5 to 10 days later. However, this technique cannot differentiate HZ from herpes simplex infection, and lack of experience with collection or interpretation of the Tzanck smear limits its usefulness.

Serologic testing. Serology has limited utility in the diagnosis of acute HZ, but may provide a retrospective diagnosis, if needed. In a study of 260 patients older than 50 years with clinically diagnosed acute HZ, varicella zoster IgA or IgM was positive in 61% of patients at the time of presentation, and in 91% of patients 5 to 10 days later.

Viral culture. Obtaining a viral culture of varicella zoster is another option, but it is not recommended, as sensitivity is poor and incubation requires several days.

The course of illness, and risk of complications
For some patients, the acute pain and hypersensitivity at the site of the rash resolve in several days; for others, this may take several weeks or more. One recent study found a median of 32.5 days for pain duration in patients ages 50 and older. The suffering can last far longer, however, if complications arise.

Postherpetic neuralgia (PHN), a chronic and often debilitating condition with pain that can last months, or even indefinitely, affects about 10% to 15% of patients with HZ. Risk factors for the development of PHN include advanced age, female sex, presence of a prodrome, severe acute HZ pain, and a severe rash.

Trigeminal nerve involvement. HZ affects the first branch of the trigeminal nerve in about 10% to 15% of patients. In such cases, the rash may erupt on the forehead, periorcular area, and nose. Patients with trigeminal nerve involvement are at significant risk for ocular complications (HZ ophthalmicus), including keratitis, iritis, and possible vision loss, and should be treated and referred to an ophthalmologist without delay.

In addition to these complications, others reported in a review of 859 patients include bacterial skin infection, motor neuropathy, and, rarely, meningitis and HZ oticus. Advanced age markedly increased the likelihood of complications.
Initiate treatment without delay
Multiple randomized controlled clinical trials have demonstrated the efficacy of oral antiviral treatment in reducing the duration of viral shedding, accelerating rash healing, and reducing the severity and duration of acute HZ pain. In all the studies, however, antiviral therapy was started within 72 hours of the onset of the rash; the efficacy of initiating antiviral treatment after >72 hours has not been systematically studied. When it’s not possible to begin therapy within this time frame, however, many experts recommend initiating therapy as soon as possible thereafter.

Three antiviral agents—acyclovir, famciclovir, and valacyclovir—have been approved by the US Food and Drug Administration to treat HZ. Evidence suggests that famciclovir and valacyclovir have comparable efficacy with regard to resolution of both the rash and the acute pain, and result in more rapid pain resolution compared with acyclovir. Famciclovir and valacyclovir also offer simpler dosing schedules—both are taken 3 times a day, while acyclovir requires 5 daily doses—but they are significantly more expensive (TABLE).

Oral antiviral therapy is strongly recommended for patients who are older than 50 and those who have moderate-to-severe pain or rash—or whose rash appears somewhere other than the trunk. But given the safety of oral antiviral agents, treatment can be considered for younger patients and those with milder cases of HZ, as well. (Routine use of antiviral agents is not indicated for unexplained unilateral pain, as varicella zoster infection without the classic rash [zoster sine herpete] is a rare cause.)

Results regarding the efficacy of oral antiviral agents for reducing the duration of chronic pain and preventing PHN are mixed. A recent Cochrane review concluded that oral acyclovir does not significantly reduce the incidence of PHN and that there is insufficient evidence to determine if other antivirals do.

Add a corticosteroid?
The evidence is mixed
Oral corticosteroids have been studied as an adjunct to antiviral therapy for the treatment of HZ. One clinical trial of 208 immunocompetent adults older than 50 found that the addition of a 21-day prednisone taper to acyclovir led to accelerated healing of cutaneous lesions, cessation of analgesic use, and return to normal activities and uninterrupted sleep. However, this study and another randomized trial of oral corticosteroids did not show that steroids had any effect on longer-term pain relief or the development of PHN. A recent Cochrane review concluded that there is insufficient evidence that corticosteroids are safe or effective in the prevention of PHN. Given the potential adverse effects of oral corticosteroids, their use should be weighed carefully.

Give analgesics for shingles pain
Many clinical trials have looked at the efficacy of different analgesics in the treatment of PHN, but data regarding analgesics for the treatment of acute HZ pain are limited. One RCT of 87 patients older than 50 divided participants into 3 groups: One group took controlled-release oxycodone, another received a placebo, and the third group took gabapentin. (The study did not include patients with...
Reserve opioids for patients with moderate-to-severe pain; those with milder pain would likely benefit from nonnarcotic analgesics.

The researchers found that the oxycodeone significantly reduced acute HZ pain during the first 2 weeks of treatment as compared with placebo or gabapentin. There was no statistically significant reduction in pain for the gabapentin group, compared with those on placebo. The oxycodeone group did have the highest dropout rate (27.6% vs 6.9% for the placebo group), however, primarily because of constipation. This study showed that narcotic analgesics are effective and relatively well tolerated for the treatment of acute HZ pain.

Because severe pain with acute HZ is a well-established risk factor for the development of PHN, there is interest in determining whether effective pain control in the acute setting decreases the risk of chronic pain. One placebo-controlled trial of 72 patients older than 60 years found that 25 mg amitriptyline daily, started within 48 hours of rash onset and continued for 90 days, reduced pain prevalence by more than half at 6 months from diagnosis. This study did not control for the use of antiviral agents, however, so further investigation is needed.

CASE Jane T began a course of antiviral therapy with valacyclovir shortly after her rash appeared, and continued to take oral tramadol for the pain. Her rash and pain level improved over the next several days, and within 2 weeks she was fully recovered.

Prevention: Vaccination holds the key

HZ is contagious and can cause primary varicella in people who are susceptible. Indeed, one study found that 15.5% of susceptible household contacts developed varicella after exposure to HZ. Advise patients with HZ to avoid contact with those at high risk for severe varicella—including pregnant women, premature infants, and immunocompromised individuals of all ages—until their lesions are crusted. They can further avoid transmission by keeping the lesions covered.

Increased use of the HZ vaccine, however, is the key to prevention of shingles. The Centers for Disease Control and Prevention (CDC) recommends Zostavax, a live attenuated varicella zoster vaccine given as a single subcutaneous injection, for people ages 60 and older. Compared with the varicella vaccines designed for children, Zostavax has a significantly higher potency in order to elicit a significant and durable response in older adults.

The vaccine is generally safe, with a mild injection site reaction being the most common adverse event. No evidence exists of transmission of virus from vaccine recipients to contacts. Like other live virus vaccines, Zostavax is contraindicated in pregnant women and immunocompromised patients. It can be given to patients regardless of their history of chickenpox or previous episodes of HZ, as studies have shown that the recurrence rate for HZ is similar to the rate for initial episodes.

How well does it work? In a Shingles Prevention Study Group trial of 38,546 people 60 years of age or older, the vaccine reduced the incidence of HZ by 51% and the incidence of PHN by 67% over a 3-year follow-up period. The vaccine was most effective for the prevention of HZ in the 60- to 69-year age group, but there was no significant difference in its efficacy in preventing PHN or reducing the burden of illness (a measure based on the incidence, severity, and duration of pain and discomfort) in 60- to 69-year-olds vs those ages 70 and older. An analysis by the CDC suggests that approximately 17 people would need to be vaccinated with Zostavax to prevent one case of HZ, and approximately 31 people would need to be vaccinated to prevent one case of PHN.

Ongoing studies are examining the safety and efficacy of Zostavax for patients ages 50 to 59. Although results thus far look promising, there is no recommendation for routine vaccination for this age group, and insurance companies do not routinely cover the cost of vaccinating them.

While primary care physicians generally favor the concept of HZ vaccination, a CDC survey conducted in 2007—a year after the vaccine received FDA approval—found that only 1.9% of eligible patients received the vaccine. Physicians cite concerns about re-
imbursement as a barrier to its use.28

Zostavax is not covered by Medicare Part B, in contrast to other adult vaccines, such as influenza and pneumococcal.29 However, the HZ vaccine is covered by many private insurers, as well as by Medicare Part D. Advise patients to check with their insurance carrier for specific details regarding their coverage, as some plans require the patient to purchase the vaccine from a pharmacy prior to administration in a physician’s office. JFP

References
20. Lu PJ, Euler GK, Jumaan AO, et al. Herpes zoster vaccination, only 1.9% of eligible patients receive the vaccine. Physicians cite concerns about reimbursement as a barrier to its use.