MANAGEMENT OF HERPES ZOSTER AND POSTHERPETIC NEURALGIA IN ELDERLY PATIENTS

Herpes zoster (HZ) is the clinical reactivation and spread of Varicella-zoster virus (VZV). More than two-thirds of HZ cases occur in people > 60 years. The most common complication of the reactivation of this virus is postherpetic neuralgia. This issue of CLIPS briefly summarizes an article that discusses herpes zoster and postherpetic neuralgia and offers options on treatment and prevention of these conditions in the elderly. If you need further information, please contact the Samford University Drug Information Service at (205) 726-2659.


Epidemiology of HZ

- Varicella-zoster virus is a human α-herpesvirus that has affinity for nerve tissue causing a primary infection (chicken pox) followed by a latency period.
- HZ results when the VZV is reactivated causing secondary disease.
- HZ results in inflammatory, viral and immune-response damage to the ganglion, the primary afferent nerve, and skin.
- In half of the affected patients, prodromal pain or itching occurs over several days followed by a unilateral, dermatomal vesicular rash that affects the thoracic region.
- Although scarring and pigmentation changes can occur, the rash usually heals in two to four weeks.
- The trigeminal nerve in the ophthalmic division is the second most commonly affected location.
- HZ affects patient populations from infants to adults; however, patients who are immunocompromised (e.g. malignancies, HIV, use of immunosuppressant drugs) are at greater risk than immunocompetent patients.
- Any patient who has had VZV and has a decline in that specific cell-mediated immunity below a certain threshold is at risk for developing HZ.
- The current lifetime risk of developing HZ by clinical reactivation of VZV is estimated to be 20-30%.
- Complications of HZ include: postherpetic neuralgia (PHN), secondary bacterial infections, ophthalmic damage, motor paresis, cerebral angiitis, Guillain-Barré syndrome, and visceral dissemination.

Epidemiology of PHN

- PHN results from VZV-induced pathophysiological changes in the pain transmitting nerve pathway and the associated segment of the spinal cord causing ongoing neuropathic pain.
- PHN usually occurs once in a patient’s lifetime.
- Recurrence is frequent in immunocompromised patients.
- PHN usually persists three to four months after the onset of the HZ rash.
- Mortality caused by HZ usually occurs in patients >65 years and is estimated at 0.6-1 per million population per year.

Prevention

- Vaccination of young children is effective in the prevention of varicella and HZ.
- An increase incidence in HZ has not been observed as a result of the routine vaccination.
- Furthermore, it has been hypothesized through observation of immunocompromised children that the incidence of HZ may actually decrease after vaccination.
- In subjects 70 years or greater, the vaccine was shown to be less effective in reducing the incidence of HZ; however, protective effects against PHN and pain were maintained.
- The Center for Disease Control and Prevention recommends that adults >60 years who are immunocompetent be vaccinated against HZ with one dose for all adults even if they have experienced shingles.
The vaccination is indicated as prevention of HZ and PHN rather than as a therapeutic intervention.

Prevention of PHN once HZ onset occurs and up to six months after the HZ infection can be achieved by using antiviral drugs with or without concomitant oral corticosteroids.

Amitriptyline has been shown in a small placebo-controlled study to reduce the risk of PHN when administered during acute HZ.

Management of PHN

In most patients, there is more than one mechanism of PHN involved; because of this, combination of two or more analgesic agents will often lead to greater pain relief and fewer side effects (smaller doses of each used) than monotherapy.

The use of combinations of two or three drugs from different classes may be more beneficial for pain relief than a stepwise approach with single agents.

Treatment of PHN consist of three main classes of oral medications and two categories of topical medications.

- Oral medications: Serotonin/norepinephrine modulating antidepressants, calcium-modulator antiepileptics, tramadol and opioids
- Topical medications: Capsaicin and lidocaine

These classes of medications all have a different mechanism to improve PHN:

- TCAs (amitriptyline, desipramine, nortriptyline [10-25 mg QHS for 6-8 weeks; Max 75-150 mg/day for 1-2 weeks]): Potentiation of the effect of CNS pain-modulating pathways is caused by inhibition of the reuptake of monoaminergic transmitters. They also block voltage-dependent sodium channels.

- Antiepileptics (gabapentin [100-300 mg QHS for 3-6 weeks; Max 1800 mg/d for 1-2 weeks] and pregabalin [50 mg TID for 2 weeks; Max 600 mg/d for 1-2 weeks]): Act on calcium channels on the spinal presynaptic terminals of the primary afferent nociceptive neurons.

- Tramadol (50 mg daily or BID for 4 weeks; Max 400 mg/d for 4 weeks) and strong opioids (5-15 mg Q4h prn for 4-6 weeks; No maximum): Tramadol is an opioid µ receptor agonist and acts on the norepinephrine and serotonin reuptake inhibitor. Using the opioid analgesics is controversial but positive results have been reported and pain can be successfully and safely treated on a long-term basis.

- Capsaicin (0.075% applied 3-4 times/d): A transient receptor potential vanilloid 1 (TRPV1) agonist. TRPV1 is found on the terminals of primary nociceptive afferents. However, the repeated or prolonged use of the product can inactivate the receptive terminals on nociceptors.

- Lidocaine (5% patch with max of 3 daily for a max of 12 hours for 2 weeks): A local anesthetic that works by blocking voltage-dependent sodium channels. May be effective because in vitro studies have shown that impulses caused by PHN pain are abolished by lower concentrations than required to block normal axonal conduction.

Since life-threatening interactions can occur with some of these combinations, advantages of these combinations should be weighed against the risk.

Based on recent study results, an opioid combined with an antiepileptic indicates a potential advantage over other early combination treatments.

Summary

- VZV is a human α-herpesvirus that has affinity for nerve tissue causing a primary infection (chicken pox) followed by a latency. HZ results when the VZV is reactivated causing secondary disease.

- HZ affects patient populations from infants to adults; however, patients who are immunocompromised (e.g. malignancies, HIV, use of immunosuppressant drugs) are at greater risk than immunocompetent patients.

- Mortality caused by HZ usually occurs in patients ≥65 years and is estimated at 0.6-1 per million population per year.

- In subjects 70 years or greater, the vaccine was shown less effective in reducing the incidence of HZ; however, protective effects against PHN and pain were maintained.

- The Center for Disease Control and Prevention recommends that adults ≥60 years who are immunocompetent be vaccinated against HZ with one dose for all adults even if they have experienced shingles.

- The use of combinations of two or three drugs from different classes may be more beneficial for pain relief than a stepwise approach with single agents.

Prepared by: Natalie Hunley, Pharm.D. Candidate
Reviewed by: Maisha Kelly Freeman, Pharm.D., BCPS