Review Article

Prevention & Management of Herpes Zoster- an Update

A K M Rejaul Haque[1], A Sultana[2], A Habib[3], ASM Zakaria[4]

Abstract:

Herpes zoster (commonly referred to as "shingles") results from reactivation of the varicella-zoster virus infection, or chickenpox. Whereas varicella is generally a disease of childhood, herpes zoster becomes more common with increasing age. Factors that decrease immune function, such as human immunodeficiency virus infection, chemotherapy, malignancies and chronic corticosteroid use, may also increase the risk of developing herpes zoster. Reactivation of latent varicella-zoster virus from dorsal root ganglia is responsible for the classic dermatomal rash and pain that occur with herpes zoster. Burning pain typically precedes the rash by several days and can persist for several months after the rash resolves. With postherpetic neuralgia, a complication of herpes zoster, pain may persist well after resolution of the rash and can be highly debilitating. Although the diagnosis of the conditions is generally straightforward, treatment can be frustrating for the patient and physician. Approaches to management include treatment of the herpes zoster infection and associated pain, prevention of postherpetic neuralgia, and control of the neuropathic pain until the condition resolves. Herpes zoster is contagious to those who have not had varicella or have not received the varicella vaccine. The role of the varicella vaccine in preventing herpes zoster is uncertain, but is being studied. The management of herpes zoster is challenging because many patients develop troublesome complication. So, appropriate management of herpes zoster is very important to avoid complication. On the other hand prevention is better than cure. Immunization with varicella zoster virus vaccine may boost humoral and cell mediated and decrease the incidence of zoster in population. So effectiveness of a vaccination program need to be evaluated.immunity

1. Dr. A K M Rejaul Haque, Assistant Professor, Dept of Dermatology and Venereology, BSMMU, Dhaka.
2. Dr. Abida Sultana, Assistant Professor, Dept of Dermatology and Venereology, BSMMU, Dhaka.
3. Dr. Ahsan Habib, Assistant Professor, Dept of Neurology, BSMMU, Dhaka.
4. Dr. ASM Zakaria, Dept of Dermatology and Venereology, BSMMU, Dhaka.

Corresponding author: Dr. A K M Rejaul Haque, Assistant Professor, Dept of Dermatology and Venereology, BSMMU, Dhaka.

Key words: prevention of herpes zoster, management of herpes zoster.

Introduction:

Herpes zoster is a sporadic disease with an estimated lifetime incidence of 10 to 20 percent. The incidence of herpes zoster increases sharply with advancing age, roughly doubling in each decade past the age of 50 years. Herpes zoster is uncommon in persons less than 15 years old.[1] In a recent study, patients more than 55 years of age accounted for more than 30 percent of herpes zoster cases despite representing only 8 percent of the study population. The normal age-related decrease in cell-mediated immunity is thought to account for the increased incidence of varicella-zoster virus reactivation.[2] Patients with disease states that affect cell-mediated immunity, such as human immunodeficiency virus (HIV) infection and certain malignancies, are also at increased risk. Chronic corticosteroid use, chemotherapy and radiation therapy may increase the risk of developing herpes zoster.[3]

The incidence of herpes zoster is up to 15 times higher in HIV-infected patients than in uninfected persons, and as many as 25 percent of patients with Hodgkin's lymphoma develop herpes zoster. The occurrence of herpes zoster in HIV-infected patients does not appear to increase the risk of acquired immunodeficiency syndrome (AIDS) and is less dependent on the CD4 count than AIDS-related opportunistic infections.[4,5] There is no evidence that herpes zoster heralds the onset of an underlying malignancy. Race may influence susceptibility to herpes zoster. Blacks are one fourth as likely as whites to develop this condition.[6] Although herpes zoster is not as contagious as the primary varicella infection, persons with reactivated infection can transmit varicella-zoster virus to nonimmune contacts. Household transmission rates have been noted to be approximately 15 percent. About 20 percent of patients with herpes zoster develop postherpetic neuralgia.[7] The most established risk factor is age; this complication occurs nearly 15 times more often in patients more than 50 years of age. Other possible risk factors for the development of post-herpetic neuralgia are ophthalmic zoster, a history of prodromal pain before the appearance of skin lesions and an immunocompromised state.[8]

Pathophysiology:

Varicella-zoster virus is a highly contagious DNA virus. Varicella represents the primary infection in the nonimmune or incompletely immune person. During the primary infection, the virus gains entry into the sensory dorsal root ganglia. How the virus enters the sensory dorsal

root ganglia and whether it resides in neurons or supporting cells are not completely understood. The varicella-zoster virus genome has been identified in the trigeminal ganglia of nearly all seropositive patients.[9]

The virus remains latent for decades because of varicella-zoster virus-specific cell-mediated immunity acquired during the primary infection, as well as endogenous and exogenous boosting of the immune system periodically throughout life.8 Reactivation of the virus occurs following a decrease in virus-specific cell-mediated immunity. The reactivated virus travels down the sensory nerve and is the cause for the dermatomal distribution of pain and skin lesions. The pathophysiology of postherpetic neuralgia remains unclear. However, pathologic studies have demonstrated damage to the sensory nerves, the sensory dorsal root ganglia and the dorsal horns of the spinal cord in patients with this condition.[10]

Clinical presentation:

The initial rash is erythematous, with multiple maculopapular lesions that subsequently become vesicular. New crops of vesicles may continue to appear for up to seven days. After a few days, the vesicular fluid becomes cloudy (i.e,pustulation). Finally, the lesion forms a crust that falls off after two to three weeks. The rash may leave scarring and changes in pigmentation. The skin eruption usually is limited to a single dermatome; the most commonly involved dermatomes are the thoracolumbar region and the face. Lesions may involve more than one dermatome and occasionally may cross the midline.[11]

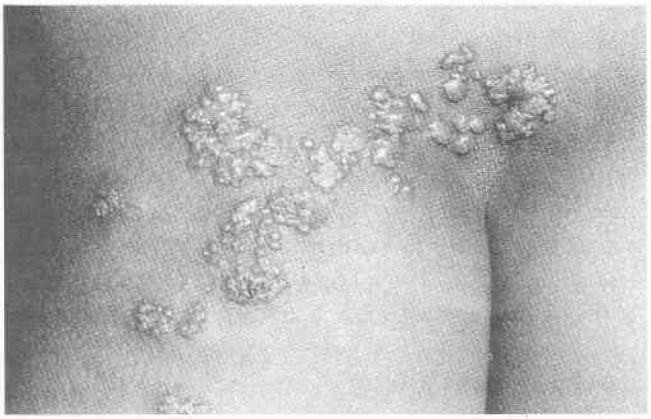

Figure 1: Typical dermatomal rash with hemorrhagic vesicles on the lower trunk of a patient with herpes zoster.

Diagnosis of Herpes zoster

The dermatomal pattern of distribution and the appearance of the herpes zoster rash are so distinctive that the diagnosis usually is clear. In cases where the diagnosis is in doubt, polymerase chain reaction (PCR) techniques are the most sensitive and specific diagnostic tests; however, these techniques are not widely available. PCR techniques detect the varicella DNA in fluid taken from the vesicles. Viral culture has a low sensitivity because the Herpes virus is labile and difficult to recover from the vesicular fluid. The direct immunofluorescent antigen-staining test has a higher sensitivity and is more rapid than culture; it provides an alternative diagnostic test when PCR is not available.1-3

Table-1: Sensitivity and specificity of tests used to diagnose Herpes Zoster 1-3

Tests	Sensitivity (%)	Specificity(%)
Immunofluorescent antigen staining	77 to 82	70 to 76
Polymerase chain reaction	94 to 95	100
Varicella Zoster specific immunoglobulin M	48 to 61	—
Virus culture	20	100

Prevention of Herpes Zoster

Immunization with Varicella Zoster Virus vaccine may boost humoral and cell mediated immunity and decrease the incidence of Zoster in populations with declining Varicella Zoster Virus specific immunity. Eradication of varicella with the vaccine should, in the long run, result in fewer cases of herpes zoster because the incidence of reactivation of the vaccine is lower than that of the virus. Because of the varicella vaccine, fewer patients will develop immunity from contact with infectious cases of the virus, potentially increasing the incidence of reactivation, at least in the short term.[4]

A double-blind, placebo controlled study[5] of varicella vaccine in patients older than 60 years showed a 61 percent reduction in pain and discomfort from herpes zoster, a 51 percent reduction in the incidence of herpes zoster, and a 66.5 percent reduction in the incidence of postherpetic neuralgia. Before a recommendation to vaccinate middle-aged adults is made, future risk of herpes zoster in previously vaccinated adults and the cost-effectiveness of a vaccination program need to be evaluated. Ultimately, when wild-type varicella virus infection decreases to minimal levels, the incidence of herpes zoster will decrease as well. Individuals at high risk for reactivation of Varicella Zoster Virus infection oral Acyclovir can reduce the incidence of Herpes Zoster.[5]

Management of Herpes Zoster

Treatment of herpes zoster with antiviral medication appears to be more effective than treatment with corticosteroids.

Antiviral therapy

Three antiviral drugs are available for the treatment of herpes zoster: acyclovir, famciclovir and valacyclovir. Acyclovir, in its generic form, is significantly less expensive than famciclovir or valacyclovir. Acyclovir accelerates resolution of all pain endpoints, especially in patients older than 50 years.[7] Famciclovir, given within 72 hours of the onset of the rash and for seven days, hastens the healing of herpes zoster by one to two days; however, acute pain is diminished only in patients with more than 50 lesions.[8] No differences have been found between famciclovir and valacyclovir.[9] These medications are safe and well tolerated, with minimal side effects (e.g., headache, nausea). Valacyclovir and famciclovir usually

are preferred because they are administered three times daily as opposed to acyclovir, which must be given five times daily.[10]

Table-2: Antiviral medications used to Treat Herpes Zoster 10

Medications	*Dosages*
Acyclovir	800 mg five times daily for seven days
Famciclovir	500 mg three times daily for seven days
Valacyclovir	1000 mg three times daily for seven days

Table-3: Treatment options for Postherpetic Neuralgia

Medication	*Dosage*
Topical agents	
Capsaicin cream	Apply to affected area three to five times daily.
Lidocaine patch	Apply to affected area every 4 to 12 hours as needed.
Tricyclic antidepressants	
Amitriptyline	10 to 25 mg orally at bedtime; increase dosage by 25 mg every 2 to 4 weeks until response is adequate, or to maximum dosage of 150 mg per day.
Nortriptyline	10 to 25 mg orally at bedtime; increase dosage by 25 mg every 2 to 4 weeks until response is adequate, or to maximum dosage of 125 mg per day.
Imipramine	25 mg orally at bedtime; increase dosage by 25 mg every 2 to 4 weeks until response is adequate, or to maximum dosage of 150 mg per day.
Desipramine	25 mg orally at bedtime; increase dosage by 25 mg every 2 to 4 weeks until response is adequate, or to maximum dosage of 150 mg per day.
Anticonvulsants	
Phenytoin	100 to 300 mg orally at bedtime; increase dosage until response is adequate or blood drug level is 10 to 20 g per mL (40 to 80 mo l per L).
Carbamazepine	100 mg orally at bedtime; increase dosage by 100 mg every 3 days until dosage is 200 to 50.8 mol per L).
Gabapentin	100 to 300 mg orally at bedtime; increase dosage by 100 to 300 mg every 3 days until dosage is 300 to 900 mg three times daily or response is adequate. (Drug levels for clinical use are not available.)

There are no data examining the effect of antiviral treatment given more than 72 hours after the onset of the herpes zoster rash. The "50-50-50 rule" can be used as a treatment guide: 50 hours or less since onset of lesions, 50 years or older, and 50 or more lesions.[12]

Steroid therapy- Two large randomized, double-blind, placebo controlled studies[11,12] evaluated 21 days of corticosteroids for the management of herpes zoster.[11,12] One study found that patients treated with corticosteroids and acyclovir had a greater reduction in pain on days 7 and 14, but at day 21 there was no difference.[11] The second study12 found that corticosteroids combined with acyclovir did not affect cutaneous healing but did result in a significant benefit in quality of life at day 30, including less time returning to normal activity and uninterrupted sleep.[12] Many patients with chronic diseases such as diabetes, renal insufficiency, and hypertension were excluded from this study, limiting its applicability. Overall, it remains doubtful that the risks associated with steroids warrant these minimal benefits. Foscarnet can be given I/V for Acyclovir resistant strains of Varicella Zoster Virus infection.[6] In immunosuppressed patients I/V Acyclovir and recombinant interferon alpha- 2a to prevent dissemination of herpes zoster.6 NSAID, gabapentin or pregabalin may be used to reduce pain in herpes zoster and antibiotic can be used to prevent secondary bacterial infection.[12]

Conclusion:

The treatment of herpes zoster should occur in conjunction with appropriate education and support from the health care provider. Careful explanation of the disease, including the risk of viral transmission to individuals who have not had chickenpox, and of the proposed treatment plan is essential for adherence to therapy and is beneficial to patient well-being; for example, providing reassurance and education can dispel myths and fears about herpes zoster and its implications for the patient's health. Encouragement, reassurance, and advice on quality of life are also important and include supporting adequate nutrition and optimal levels of mental, physical, and social activity. Patients should be told to keep the rash clean and dry to reduce the risk of bacterial superinfection, to avoid use of topical antibiotics and of dressings with adhesive that can cause irritation and delay rash healing, and to inform their physician if a secondary increase in temperature develops, which is often an indication of bacterial infection. For some patients, discomfort may be reduced by sterile wet dressings.

References:

1. Bezold GD, Lange ME, Gall H, Peter RU. Detection of cutaneous Varicella Zoster virus by immunofluorescence versus PCR. Eur J Dermatol 2001;11:108-11.
2. Sauerbrei A, Eichhorn U, Schacke M, Wutzler P. Laboratory diagnosis of Herpes Zoster. J Clin Virol 1999;14:31-6.

3. Sauerbrei A, Sommer M,Eichhorn U, Wutzler P. Laboratory diagnosis of Herpes Zoster: virology or serology? Med Klin (Munich) 2002;97:123-7.
4. Edmunds WJ, Brisson M. The effect of vaccination on the epidemiology of Herpes Zoster virus. J Inffect 2002;44:211-9.
5. Oxman MN, Levin MJ, Johnson GR, Schmader KE, Straus SE,Gelb LD,et al. A vaccine to prevent Herpes Zoster and postherpetic neuralgia in older adults. N Engl J Med 2005;352:2271-84.
6. Klaus Wolf, Richard Allen Johnson, Dick Suurmond et al. Fitzpatrick's Color Atlas and Synopsis of clinical dermatology, 6th edition, 2009;822-826.
7. Wood MJ, Kay R, Dworkin RH, Soong SJ, Whitley RJ. Oral acyclovir therapy accelerates pain reduction in patients with herpes zoster a meta-analysis of placebo-controlled trials. Clin Infect Dis 1996;22:341-7.
8. Tyring S, Barbarash RA, Nahlik JE, Cunningham A, Marley J, Heng M, et al. Famciclovir for the treatment of acute herpes zoster, effects on acute disease and post-herpetic neuralgia. A randomized, double- blind, placebo- control trial. Ann Intern Med 1995;123:89-96.
9. Tyring SK, Beutner KR, Tucker BA, Anderson WC, Crooks RJ. Antiviral therapy for herpes zoster randomized controlled clinical trial of acyclovir and famciclovir therapy in immunocompetent patients 50 years and older. Arch Farm Med 2000;9:863-9.
10. Games WD, Berger TD, Elston DM, Andrews diseases of the skin, Clinical Dermatology, I Sunderelsvier, Philadelphia, USA,Tenth edition, 2006;380-383.
11. Wood MJ, Johnson RW, McKendrick MW, Taylor J, MandalBK, Crooks RJ. A randomized trial of Acyclovir for 7 days or 21 days with or without prednisolone for the treatment of acute herpes zoster. N Eng J Med 1994;330:896-9000.
12. Whitley RJ, Weiss H, Gnann JW, Jr, Tyring S, Mertz GJ, Pappas PG, et al. Acyclovir with or without prednisolone for the treatment of herpes zoster. A randomized placebo-controlled trial. Ann Intern Med 1996; 125:376-83.