

Clinical Evidence Handbook

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Postherpetic Neuralgia

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Pain that occurs after resolution of acute herpes zoster infection can be severe. It may be accompanied by itching and follows the distribution of the original infection. All definitions of postherpetic neuralgia are arbitrary and include development from one to six months after the rash. For clinical trials, neuralgia of three months or more has become the most common definition, because resolution of neuralgia after three months is slow.

- The main risk factor for postherpetic neuralgia is increasing age. The condition is uncommon in persons younger than 50 years. However, among persons who have had acute herpes zoster, it develops in 20 percent of those 60 to 65 years of age and in greater than 30 percent of those older than 80 years.

- Up to 2 percent of persons with acute herpes zoster may continue to have postherpetic pain for five years or more.

Oral antiviral agents (acyclovir, famciclovir, valacyclovir, and netivudine), taken during acute herpes zoster infection, may reduce the duration of postherpetic neuralgia compared with placebo.

- We do not know whether topical antiviral drugs, tricyclic antidepressants, or corticosteroids taken during an acute attack reduce the risks of postherpetic neuralgia, as we found few good-quality studies.

- Corticosteroids may cause dissemination of herpes zoster infection.

- We do not know whether the use of dressings, oral opioids, or gabapentin during an acute attack reduces the risk of postherpetic neuralgia, as we found no studies.

- There is limited evidence that gabapentin and oxycodone may reduce the acute pain of herpes zoster.

- Gabapentin, tricyclic antidepressants (amitriptyline, nortriptyline), and some opioids (oxycodone, morphine, methadone) may reduce pain at up to eight weeks in

persons with established postherpetic neuralgia compared with placebo.

- Topical lidocaine may be more effective than placebo in treating postherpetic neuralgia.

- Adverse effects of tricyclic antidepressants are dose-related and may be less frequent in postherpetic neuralgia compared with depression, as lower doses are generally used.

- Opioid analgesic drugs are likely to be effective in reducing pain associated with postherpetic neuralgia, but they can cause sedation and other well-known adverse effects.

- We do not know whether dextromethorphan is effective at reducing postherpetic neuralgia.

- We do not know whether topical counterirritants such as capsaicin reduce postherpetic neuralgia.

- The herpes zoster vaccine should be used for the primary prevention of herpes zoster and postherpetic neuralgia in persons older than 60 years.

- We do not know whether serotonin-norepinephrine reuptake inhibitors (duloxetine, venlafaxine) or selective serotonin reuptake inhibitors are effective at reducing postherpetic neuralgia.

Definition

Postherpetic neuralgia is pain that often follows resolution of acute herpes zoster infection and healing of the zoster rash. Herpes zoster is caused by reactivation of latent varicella zoster virus (human herpes virus 3) in persons who have been rendered partially immune by a previous case of chickenpox. Herpes zoster infects the sensory ganglia and their areas of innervation. It is characterized by pain in the distribution of the affected nerve, and crops of clustered vesicles over

Clinical Questions

What are the effects of interventions aimed at preventing herpes zoster and subsequent postherpetic neuralgia?

Beneficial Herpes zoster vaccines

What are the effects of interventions during an acute attack of herpes zoster aimed at preventing postherpetic neuralgia?

Unknown effectiveness Antiviral agents (oral acyclovir, famciclovir, valacyclovir, netivudine)
Antiviral agents (topical idoxuridine)
Dressings
Gabapentin
Opioid analgesic drugs (oral)
Tricyclic antidepressants (amitriptyline)

Likely to be ineffective or harmful Corticosteroids

What are the effects of interventions to relieve established postherpetic neuralgia after the rash has healed?

Beneficial Gabapentin
Tricyclic antidepressants

Likely to be beneficial Lidocaine (topical)
Oral opioid analgesic drugs (oxycodone, morphine, methadone, tramadol)

Unknown effectiveness Capsaicin (topical)
Dextromethorphan
Selective serotonin reuptake inhibitors
Serotonin-norepinephrine reuptake inhibitors

the area. Pain may occur days before rash onset, or the rash may be absent (zoster sine herpete), making the diagnosis difficult.

Postherpetic neuralgia is thought to arise following nerve damage caused by herpes zoster. Postherpetic neuralgia can be severe, accompanied by itching, and it follows the distribution of the original infection. All definitions of postherpetic neuralgia are arbitrary and include development from one to six months after the rash. Neuralgia of three months or more has become the most common definition in clinical trials because resolution of neuralgia after three months is slow. Thus, the number of persons required for parallel and crossover trial designs is limited, and there is less risk of a period effect in a crossover trial.

Incidence and Prevalence

In a U.K. general practice survey of 3,600 to 3,800 persons (321 cases of acute herpes zoster), the annual incidence of herpes zoster was 3.4 out of 1,000; however, the incidence varied with age. Herpes zoster was relatively

uncommon in persons younger than 50 years (less than two out of 1,000 per year), but rose to between five and seven out of 1,000 per year in persons 50 to 79 years of age, and 11 out of 1,000 in persons 80 years and older. A population-based study in the Netherlands reported a similar incidence (3.4 out of 1,000 per year) and a similar increase of incidence with age (three to 10 out of 1,000 per year in persons older than 50 years).

Prevalence of postherpetic neuralgia depends on when it is measured after acute infection. There is no agreed upon time period for diagnosis. About 10 percent of all ages have postherpetic neuralgia one month after the rash, but because there is a direct relationship to age, about 50 percent will continue to be affected at 60 years of age.

Etiology and Risk Factors

The main risk factor for postherpetic neuralgia is increasing age. In the U.K. general practice study there was little risk in those younger than 50 years, but postherpetic neuralgia developed in greater than 20 percent

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of persons 60 to 65 years of age who had had acute herpes zoster, and in 34 percent of those older than 80 years. No other risk factor has been found to consistently predict which persons with herpes zoster will experience continued pain. In a general practice study in Iceland (421 persons followed for up to seven years after an initial episode of herpes zoster), the risk of postherpetic neuralgia was 1.8 percent (95% confidence interval, 0.6 to 4.2 percent) for persons younger than 60 years, and the pain was mild in all persons. The risk of severe pain after three months in persons older than 60 years was 1.7 percent (95% confidence interval, 0 to 6.2 percent).

Other risk factors for postherpetic neuralgia are severe pain with herpes zoster, greater rash severity, increased neurologic abnormalities in the affected dermatome (sensory loss), the presence of a prodrome, a more pronounced immune response, and psychosocial factors.

Prognosis

About 2 percent of persons with acute herpes zoster in the U.K. general practice survey had pain for greater than five years. Prevalence of pain decreases as time elapses after the initial episode. Among 183 persons older than 60 years in the placebo arm of a U.K. trial, the prevalence of pain was 61 percent at one month, 24 percent at three months, and 13 percent at six months after acute infection. In one randomized controlled trial, the prevalence of postherpetic pain in the placebo arm at six months was 35 percent in 72 persons older than 60 years. After postherpetic neuralgia has persisted for more than one year, about 50 percent of persons will have significant pain, and 50 percent will recover or have pain control with medication at a median of two years of follow-up.

EDITOR'S NOTE: Idoxuridine and netivudine are not available in the United States.

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