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FPIN's Clinical Inquiries

Treatment of Herpes Zoster

Clinical Question

What is the best treatment for patients with an outbreak of herpes zoster?

Evidence-Based Answer

Resolution of acute pain related to herpes zoster is accelerated with any of the following: oral acyclovir (Zovirax) 800 mg five times daily for seven days; valacyclovir (Valtrex) 1,000 mg three times daily for seven days; or famciclovir (Famvir) 750 mg once daily, 500 mg twice daily, or 250 mg three times daily for seven days. (Strength of recommendation: A)

Famciclovir and acyclovir are similarly effective at improving the rate of lesion healing. (Strength of recommendation: B)

Oral valacyclovir may be slightly superior to acyclovir for resolution of acute pain. (Strength of recommendation: B)

Acyclovir 800 mg five times daily for seven to 10 days reduces the occurrence of postherpetic neuralgia. (Strength of recommendation: A)

Oral corticosteroids given during the acute phase of the illness have not been shown to reduce the incidence or severity of postherpetic neuralgia. (Strength of recommendation: B)

There is no evidence to support the use of tricyclic antidepressants or anticonvulsants for the management of herpes zoster. (Strength of recommendation: B)

Evidence Summary

Table 11-5 is a summary of the outcomes of five studies of treatment of herpes zoster patients.

Table 1

Summary of Treatment Outcomes for Herpes Zoster: Systematic Reviews and Randomized Control Trials (RCTs)

Study	Outcome
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Wood, et al ¹	Acyclovir (Zovirax) 800 mg five times daily for seven days is better (n=1076), meta-analysis
Beutner, et al ²	Valacyclovir (Valtrex) 1,000 mg three times daily for seven days is better than acyclovir 800 mg five times daily for seven days for resolution of pain.
Tyring, et al ³	Famciclovir (Famvir) 500 mg three times daily or 750 mg three times daily for seven days increases rate of lesion healing better than placebo.
Shen, et al ⁴	Famciclovir 250 mg three times daily for seven days is equal to acyclovir 800 mg five times daily for seven days for resolution of pain and rate of lesion healing.
Shafran, et al ⁵	Famciclovir 750 mg once daily for seven days, 500 mg twice daily for seven days, 250 mg three times daily for seven days, and acyclovir 800 mg five times daily for seven days are all equally effective for resolution of pain and rate of lesion healing.

Information from references 1 through 5.

treatment of acute herpes zoster

A meta-analysis of five randomized controlled trials (RCTs) considered the time to complete resolution of acute herpes zoster pain.¹ When treatment (acyclovir 800 mg five times daily for seven days) was initiated within 48 hours, complete resolution of pain occurred sooner than with placebo (28 versus 62 days, $P < .005$). This also was true when treatment was initiated between 48 and 72 hours (28 versus 58 days, $P = .04$).

A single RCT² compared valacyclovir (1,000 mg three times daily for seven days) with acyclovir (800 mg five times daily for seven days). This study found that the mean times to complete resolution of pain were 44 days for valacyclovir and 51 days for acyclovir when treated within 48 hours ($P = .03$).² When treatment was initiated between 48 and 72 hours after the onset of symptoms, the mean times to complete resolution of pain were 36 days for valacyclovir and 48 days for acyclovir ($P = .02$).

Another RCT³ compared two dosage regimens of famciclovir (500 mg three times daily for seven days or 750 mg three times daily for seven days) with placebo in 419 adults treated within 72 hours of symptom onset. Famciclovir slightly accelerated the rate of lesion healing compared with placebo (median difference of one to two days for different doses and lesion endpoints).

In a single RCT⁴ with 55 patients, famciclovir (250 mg three times daily for seven days) was shown to have equal effectiveness to acyclovir (800 mg five times daily for seven days). This small and possibly underpowered study found that there was no significant difference regarding the median time to full lesion crusting, the rate of full crusting at day 28, the median time to resolution of acute pain, or the rate of acute pain at 28 days.

Three different dosage regimens of famciclovir (750 mg once daily for seven days, 500 mg twice daily for seven days, or 250 mg three times daily for seven days) and one regimen for acyclovir (800 mg five times daily for seven days) were compared in another RCT⁵ with 559 patients presenting within 72 hours of onset. The time to full crusting was similar (seven to eight days) for all four dosage regimens. There was no significant difference in time to acute pain resolution: 14 days for the acyclovir regimen, 17 days for famciclovir 250 mg three times daily, and 19 days for famciclovir 500 mg twice daily and 750 mg once daily).

Prevention and treatment of postherpetic neuralgia

A systematic review⁶ considered 42 RCTs of therapies to prevent or reduce the incidence of postherpetic neuralgia pain. Acyclovir (800 mg five times daily for seven to 10 days) reduced the incidence of postherpetic neuralgia pain at three months (number needed to treat [NNT] = 3.2 to 8.0).

Famciclovir reduced the duration of postherpetic neuralgia pain better than placebo.³ The time to resolution of pain in patients 50 years of age or older was significantly shorter for two dosages of famciclovir (500 mg [P = .004] or 750 mg [P = .003] given three times daily for seven days) than for placebo (63 versus 163 days).

Systemic steroids have demonstrated no additional benefit. Studies examining amitriptyline, narcotics, capsaicin, anticonvulsants, and percutaneous nerve stimulation for postherpetic neuralgia were of fair to poor quality and no conclusions could be drawn from these.

Recommendations from Others

A consensus guideline from the International Herpes Management Forum⁶ recommends antiviral therapy with valacyclovir (1,000 mg three times daily for seven days) or famciclovir (250 mg or 500 mg three times daily for seven days) for immunocompetent adults older than 50 years; treatment should be initiated within 72 hours of rash onset. Systemic oral steroids are recommended to reduce acute symptoms. It also is recommended that tricyclic antidepressants be considered to reduce the incidence of postherpetic neuralgia in older patients. Topical antiviral agents are not recommended.

Clinical Commentary

Appropriate care for patients with herpes zoster requires the entire office staff to understand the natural course of the illness and the need for early treatment (within 72 hours). Office assistants must recognize that prodromal pain symptoms or onset of rash are indications for an appointment that day to confirm the diagnosis and to begin treatment. Because the rash results in physical appearance changes, many patients have a high anxiety level about their illness. In addition, many myths exist about herpes zoster. Patient education should focus on infectivity, symptoms that require a follow-up office visit, and the importance of completing the entire course of medications.

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