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ONE MINUTE CONSULT
BRIEF ANSWERS TO SPECIFIC CLINICAL QUESTIONS

Q: Is there a role for chronic suppressive therapy in herpes simplex virus infection?

A: Yes. The primary role of chronic suppressive therapy in herpes simplex virus (HSV) infection is to decrease the frequency, severity, and duration of outbreaks, and to reduce the risk of transmitting the virus to others. It is indicated in patients with recurrent oral and genital HSV-2 infection and oral HSV-1 infection. However, there is no clear proven benefit in providing chronic suppressive therapy in recurrent genital HSV-1 infection.

WHAT IS HSV INFECTION?

HSV infection is caused by 1 of 2 types of herpes viruses: HSV-1 and HSV-2. HSV-1 primarily causes oral herpes but can also cause genital herpes. It typically manifests as cold sores or fever blisters around the mouth. Transmission usually occurs through direct contact such as kissing, or by sharing items like utensils, cosmetics, or towels. In recent years, due to changes in sexual practices, HSV-1 has been causing an increasing number of genital herpes cases.[1] HSV-2 is mainly responsible for genital herpes, resulting in sores or blisters on or around the genitals or rectum. It is mainly transmitted through sexual contact.

The initial episode of HSV infection can be categorized as either primary (ie, in patients without existing antibodies) or nonprimary (in patients with preexisting antibodies to the virus). Symptoms such as painful sores, fever, body aches, swollen lymph nodes, and headaches are more pronounced in primary infection than in nonprimary HSV-2 infection.[2] While the virus is highly contagious during outbreaks of visible sores, it can also be transmitted without any noticeable symptoms, a phenomenon known as asymptomatic shedding.[3]

doi:10.3949/ccjm.91a.23099

HOW DO YOU TREAT INITIAL HSV INFECTION?

There is no cure for HSV infection. Antiviral medications such as acyclovir, valacyclovir, and famciclovir can mitigate the severity, frequency, and duration of outbreaks and lower the risk of transmission. It is crucial to start antivirals as soon as possible, ideally within 72 hours of symptom onset.[4]

The primary objective of antiviral medications is to reduce the duration and severity of the disease by days to weeks. Oral antiviral medications have been shown to decrease the severity of symptoms, reduce the duration of pain, accelerate lesion healing, and minimize viral shedding in patients experiencing their first episode of primary genital HSV infection.[4] The US Centers for Disease Control and Prevention recommends 7 to 10 days of acyclovir 400 mg orally 3 times a day, famciclovir 250 mg orally 3 times a day, or valacyclovir 1,000 mg orally 2 times a day.[5] The dose of these medications needs to be adjusted based on the patient's creatinine clearance rate. Valacyclovir is an alternative to acyclovir, offering the advantage of more convenient administration with comparable efficacy.[4] No randomized trial has compared the efficacy with famciclovir.

WHAT IS RECURRENT HSV?

HSV can lead to recurrent outbreaks. After the initial infection, HSV remains dormant in the sensory nerve ganglia and may reactivate under stress, illness, or immunosuppression, causing subsequent outbreaks. The frequency of these outbreaks may diminish over time.[6] HSV-2 is associated with a higher rate of recurrence (a median of 4 times per year) than HSV-1 (with

TABLE 1
Episodic treatment regimens for recurrent herpes simplex virus infection

Medication	Dose and duration
Acyclovir	800 mg 3 times daily for 2 days 800 mg twice daily for 5 days
Famciclovir	1,000 mg twice daily for 1 day 500 mg once, then 250 mg twice daily for 2 days 125 mg twice daily for 5 days
Valacyclovir	500 mg twice daily for 3 days 1,000 mg once daily for 5 days

Based on information in reference 5.

TABLE 2
Chronic suppressive regimens in patients without and with HIV infection

Medication	Patients without HIV	Patients with HIV or immunosuppressive condition
Acyclovir	400 mg twice daily	400 mg to 800 mg 2–3 times a day
Valacyclovir	500 mg to 1,000 mg once daily	500 mg twice daily
Famciclovir	250 mg twice daily	500 mg twice daily

HIV = human immunodeficiency virus

Based on information in reference 5.

a median of once per year).[7] The initial treatment does not reduce the frequency of these recurrences.[8] Recurrent HSV can be managed with either episodic or chronic suppressive therapy.

HOW DO YOU DIFFERENTIATE HSV-1 AND HSV-2 INFECTION?

For patients with active genital lesions, type-specific virologic testing by culture or nucleic acid amplification should distinguish HSV-1 from HSV-2 lesions. In the absence of active genital lesions, serologic tests can help differentiate the cause of recurrent oral and genital lesions. However, because many asymptomatic people test positive for antibodies, serologic testing is not routinely indicated in the general population and should be used only to determine risk for a partner who may be discordant (ie, not previously positive for HSV-1 or HSV-2 on serologic testing).[9]

EPISODIC THERAPY VS CHRONIC SUPPRESSIVE THERAPY

Episodic treatment is self-administration of the medication at the first signs of prodromal symptoms such as tingling, paresthesia, and itching to prevent the onset of the outbreak (**Table 1**).[5] Early administration of antivirals has been shown to be beneficial.[4] Episodic therapy can shorten the time to crusting and healing of lesions and can also decrease viral shedding.[10] Episodic regimens are typically shorter in duration than initial therapy and can vary from 1 day to 5 days. Patients with human immunodeficiency virus (HIV) infection should be treated for 5 days.

For HSV-2 infection, chronic suppressive therapy is preferred over episodic therapy, as it has been linked to greater treatment satisfaction and a decreased risk and frequency of recurrence.[11] No data are available regarding its efficacy in preventing transmission among individuals with genital herpes caused by HSV-1. Because HSV-1 infection carries a lower rate of recurrent outbreaks than HSV-2, most patients with genital HSV-1 infection do not require suppressive therapy.[1]

WHICH PATIENTS BENEFIT MOST FROM CHRONIC SUPPRESSIVE THERAPY?

Unfortunately, the antiviral drugs used to treat the initial episode of HSV infection do not eradicate the latent virus, nor do they influence the risk, frequency, or severity of recurrences once the drug is discontinued. As a result, chronic suppressive therapy is recommended for patients with a history of genital HSV-2 infection who experience frequent or severe outbreaks.[4] This recommendation also extends to patients with risk factors such as ongoing immunosuppression (solid-organ transplant, bone marrow transplant, HIV) and patients with a history of genital herpes who have multiple partners or partners who are discordant.[12]

Chronic suppressive therapy has been found to reduce the frequency of genital herpes recurrences by 70% to 80%.[5,11,13] In addition to decreasing the severity of symptoms[2] and reducing the frequency of outbreaks,[13] suppressive therapy has been shown to reduce asymptomatic viral shedding, thereby decreasing the potential for transmission to HSV-uninfected sexual partners.[3]

Currently recommended agents for chronic suppressive therapy include acyclovir, valacyclovir, and famciclovir (**Table 2**).[5] Once-daily treatment with valacyclovir 500 mg has been shown to decrease the

rate of HSV-2 transmission in discordant heterosexual couples where 1 partner has a history of genital HSV-2 infection.[14]

However, for HSV-2, the question remains whether reducing the frequency of recurrences equates to a lower risk of transmission to sexual partners. Kim et al[15] found that the severity of HSV-2 infection defined as the frequency of recurrences did not help identify patients most likely to transmit the infection to a discordant partner.[15] A higher daily dose of valacyclovir (1,000 mg) is recommended in patients who have 10 or more episodes per year.[13] Higher doses are typically recommended for patients with HIV and in pregnant women to prevent neonatal herpes infections.[5] Patients should be evaluated annually for continuation of chronic suppression.[5]

THE BOTTOM LINE

Chronic suppressive therapy is recommended for patients with recurrent genital HSV infection. It is effective in decreasing the frequency and severity of symptoms, and can decrease viral shedding and transmission from HSV-2-infected patients to sexual partners. HSV-1 is associated with a lower risk of recurrent infection.[7] Current available data do not show a clear benefit of chronic suppressive therapy in patients with recurrent HSV-1 infection.

DISCLOSURES

The authors report no relevant financial relationships which, in the context of their contributions, could be perceived as a potential conflict of interest.

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