Herpes Viral Shedding Goes Beyond 10 Years

BY MIRIAM E. TUCKER
Senior Writer

WASHINGTON — High rates of both overall and subclinical viral shedding continue even beyond 10 years among people with genital herpes simplex virus type 2 infection, suggesting that there is a continued risk of transmission to sexual partners long after initial infection.

The findings, from a study of 377 healthy adults with a history of symptomatic herpes simplex virus type 2 (HSV-2) infection, "have implications for long-term management of transmission and treatment of clinical recurrences, including long-term use of antiviral medications for clinical suppression and condom use to reduce transmission to partners," Dr. Warren Phipps said at the jointly held annual Interscience Conference on Antimicrobial Agents and Chemotherapy and the annual meeting of the Infectious Diseases Society of America.

Previous studies suggest that rates of HSV-2 shedding during the first year of infection range from 9% to 40% of days sampled using polymerase chain reaction (PCR), and that clinical recurrences are common, with a median of about four outbreaks per year. Subclinical shedding during the first year is estimated to represent about 50% of days of reactivation. Much less is known about the natural history of genital herpes beyond the first year, and the available data conflict as to whether viral shedding decreases with time, noted Dr. Phipps of the University of Washington and the Fred Hutchinson Cancer Research Center, Seattle.

The study population included participants in several prospective observational studies, some of them funded by GlaxoSmithKline, conducted at two clinics from 1992 to 2008. Subjects collected swabs on at least 30 consecutive days from perianal, vulvar, cervical, penile, and/or urethral sites. They also kept symptom diaries in which they recorded the appearance of genital lesions. The swabs were tested for HSV-2 using PCR, with a positive sample defined as greater than or equal to 150 copies/mL of HSV-2 DNA from any site.

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The 377 subjects had a mean age of 39 years (range 20-76 years), were 62% female, and were 89% white. The entire group collected swabs in a total of 439 sessions with a mean of 64 days per session, for a total of 28,252 swab days. Participants were grouped as having had "less than 1 year," "1-9 years," and "10 or more years" since their initial episode.

Time since initial genital herpes episode was associated with reductions in both total and subclinical HSV-2 shedding, from 26% of sampled days within 1 year, to 16% at 1-9 years, to 14% at 10 years and beyond for total shedding, and from 19% to 8% to 4% of sampled days, respectively, for subclinical shedding. The appearance of clinical lesions dropped insignificantly with time, from 11% to 10% to 7% of sampled days for the three groups, respectively. "Although shedding was reduced, it is important to note that rates still remained high even beyond 10 years or more from the initial clinical episode," Dr. Phipps commented.

Race had a significant impact on the change in reactivation rates over time, with nonwhites having much higher rates than whites within the first year (65% vs. 26%) but dropping to a much lower level at 1-9 years (7% vs. 18%) and at 10 or more years (4% vs. 16%). Rates of subclinical shedding also decreased to a greater degree with time in blacks vs. whites.

Small but significant decreases were seen in HSV-2 DNA copy numbers over time, from 4.8 to 4.6 log10 copies/mL between the less than 1 year and 10 years or greater groups. "It is important to note that although there is no known 'infectivity threshold,' it is generally thought that virus is infectious at greater than 3 log10 copies/mL, so these titers remain in presumed infectious range remote from initial infection," he said.

Duration of any reactivation and subclinical reactivation episodes did not change over time, but the duration of clinical episodes did decrease significantly, from a median of 8.5 days within 1 year, to 5.8 days at 1-9 years, to 5.0 days at 10 years and beyond. Dr. Phipps said that he had no financial disclosures. ■

Single-Day Famciclovir Found To Match 3-Day Valacylovir

BY MIRIAM E. TUCKER
Senior Writer

WASHINGTON — Single-day famciclovir therapy was similar in safety and efficacy to a 3-day course of valacylovir in the first head-to-head comparison of the two oral medications for the treatment of recurrent genital herpes.

Previous data showed that, when taken within 6 hours of symptom onset, single-day famciclovir (Famvir, 1,000 mg b.i.d.) increased the proportion of patients with aborted episodes from 13% to 23%, and reduced healing time and duration of symptoms by 2 days, compared with placebo (Clin Infect Dis 2006;42:8-13).

Now, the findings of a multicenter, randomized, double-blind, parallel group study of 751 adults with recurrent genital herpes suggest that single-day famciclovir is as safe and effective as 3-day valacyclovir (Valtrex, 500 mg b.i.d.), Dr. Stephen Tyring said at the jointly held annual Interscience Conference on Antimicrobial Agents and Chemotherapy and the annual meeting of the Infectious Diseases Society of America.

Patients were at least 18 years of age and had experienced at least 4 outbreaks of lesions on the external genitalia or anogenital area in the preceding 12 months, with positive herpes simplex virus serology. About two-thirds were female, and most had used suppressive therapy in the previous 12 months. Of the 1,179 patients who were randomized, 751 initiated the study medication within 6 hours of their next recurrence and were included in the analysis.

The proportion of patients with aborted lesions in the intent-to-treat population was 32.7% among the 370 famciclovir patients and 33.6% among the 381 valacyclovir patients. Time to healing of nonaborted lesions was 4.25 days with single-day famciclovir and 4.08 days with 3-day valacyclovir, an insignificant difference. There were also no differences in time to resolution of burning, pain, tingling, itching, tenderness, or all symptoms together, said Dr. Tyring of the Center for Clinical Studies at Texas Medical Center, Houston.

Time to lesion healing was 4.25 days with single-day famciclovir and 4.08 days with 3-day valacyclovir.

DR. TYRING

Adverse events were reported in about one-fifth of each group, with drug-related events reported in 11% with famciclovir and 9% with valacyclovir. Headache was the most common adverse event, reported in 8% with famciclovir and 4% with valacyclovir.

Dr. Tyring receives research funding and is on the speakers bureau for Novartis, manufacturer of Famvir, and GlaxoSmithKline, manufacturer of Valtrex. ■

HSV Shedding Unaffected by Outbreak Frequency, Duration

BY HEIDI SPLETE
Senior Writer

WASHINGTON — People infected with the herpes simplex virus shed virus no matter how long they have been infected or how frequently they have outbreaks, according to data from adults aged 18 years and older with newly acquired and long-term herpes infections.

Previous studies have suggested that herpes recurrences are more frequent within the first year after infection, and that viral shedding occurs on nearly 40% of days in patients with herpes simplex virus (HSV) infection for 6 months or less, said Clare A. Brennan and Cathy K. Heitman, Ph.D., of the infectious diseases medicine development center for GlaxoSmithKline in Research Triangle Park, N.C.

But the current study is the first to show a viral shedding rate on more than 50% of days in patients with new infections, they noted.

To study the natural history of viral shedding in patients with HSV-2, the researchers conducted a post hoc analysis of a placebo group of 69 patients who were part of a larger study that compared valacyclovir, acyclovir, and placebo. The group comprised 27 patients who had had HSV-2 for 6 months or less, and 42 patients with HSV-2 for longer than 6 months and at least six recurrences per year. The new-infection group comprised 9 men and 18 women, and the established-infection group comprised 18 men and 24 women.

The researchers presented their results in a poster session at the jointly held annual Interscience Conference on Antimicrobial Agents and Chemotherapy and the annual meeting of the Infectious Diseases Society of America.

Overall, subclinical shedding was more than twice as high in patients with newly acquired infections as it was in those with established infections (31% vs. 14%, respectively).

When the researchers examined subclinical shedding as a function of HSV-2 duration, the rate of subclinical shedding was 33% in 29 patients diagnosed within a year, 14% in 17 patients infected for 1-5 years, 15% in 9 patients infected for 6-10 years, and 11% in 13 patients infected for 11 years or longer. (Complete data were not available for one patient.)

Patients with the least number of outbreaks shed virus at the highest rate, the researchers noted. The percentage of days with subclinical shedding for the patients who had 0-3, 4-5, and more than 5 outbreaks within the past 6 months was 24%, 17%, and 16%, respectively.

The results suggest that people with few HSV outbreaks or with long-term infections are not exempt from subclinical shedding, and they could still transmit the virus to an uninfected partner, the researchers noted.

The study was sponsored by GlaxoSmithKline. ■