HSV-1 Likely Cause of New Genital Infections

BY ELIZABETH MECHCATIE
Senior Writer

BETHESDA, MD. — Herpes simplex virus 1 has emerged as an important genital pathogen and is more likely than herpes simplex virus 2 to be the cause of primary genital herpes infections in young women, Sharon L. Hillier, Ph.D., said at a conference on vulvovaginal diseases.

Young, sexually active women are more susceptible to HSV-1 because most do not have protective antibodies to HSV-1 due to the dramatic drop in childhood HSV-1 infections, said Dr. Hillier, director, reproductive infectious disease research, Magee-Womens Hospital, Pittsburgh.

Among the major implications of this trend is the potential utility of the genital herpes vaccine that is being developed, since it targets only HSV-2, she pointed out.

Since current estimates of genital herpes from national seroprevalence studies include only HSV-2 infections, they "probably greatly underestimate the amount of genital herpes" in this country, Dr. Hillier said at the conference, sponsored by the American Society for Colposcopy and Cervical Pathology.

Studies documenting the emergence of HSV-1 as a cause of primary genital herpes infections date to 1990, when HSV-1 was found to have replaced HSV-2 as the most common cause of genital herpes in Scotland. Studies published in 2000 reported that HSV-1 was the cause of 85% of all primary genital HSV infections in Sweden and 70%-90% of all first episodes of genital herpes in women younger than 21 in Norway.

In the United States, a 2003 study found that the proportion of newly diagnosed genital herpes infections due to HSV-1 in a university student health service increased from 31% in 1993 to 78% in 2001.

In a recently published study, Dr. Hillier and her associates found that only 29% of a sample of college students at a University of Pittsburgh student health clinic had antibodies to HSV-1, making the majority susceptible to infection. The study enrolled 1,207 women aged 18-30 years at three different health clinics and found that the HSV-1 seroprevalence was 47% overall, but 60% at the primary care clinic and 51% at an STD clinic (Sex. Transm. Dis. 2005;32:84-9).

Their results indicated that age and number of sex partners was associated with HSV-1 seroprevalence: 38% of the women aged 18-20 years were positive for HSV-1 antibodies, increasing to 49% among those aged 21-25 years, and 64% among those aged 26-30 years. HSV-1 seroprevalence was 26% among those who previously had no sex partners, 41% among those who had one to four sex partners in their lifetime, and 53% among those who had five or more lifetime sex partners.

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DR. HILLIER

Follow-up of these women determined that cunnilingus and vaginal intercourse were risk factors for the acquisition of HSV-1 infections: Of the 516 HSV-1 seronegative women who returned for 1,833 visits, 29 acquired antibodies to HSV-1. That means that 6% of the women per year were acquiring herpes infections due to HSV-1 infection, said Dr. Hillier, also, professor of obstetrics, gynecology, and reproductive sciences, and of molecular genetics and biochemistry at the University of Pittsburgh.

When the researchers looked at sex practices, the acquisition rate for HSV-1 was highest among those who had receptive oral sex only, at 9.8 cases per 100 woman-years, compared with 1.2 per 100 woman-years among those who were not sexually active—a significant difference.

Among women having vaginal intercourse, the acquisition rate for HSV-1 was 6.8 cases per 100 woman-years, or 6.8% per year, she said. The HSV-2 acquisition rate was 5.7 cases per 100 woman-years among those reporting vaginal intercourse, but zero among those reporting receptive oral sex only.

Therefore, "women who report only oral sex are just as likely to acquire HSV-1 as women reporting vaginal sex," Dr. Hillier concluded.

These data are similar to data reported from Scotland and Finland, indicating that oral sex increases the risk of HSV-1 "and has really changed the way we have begun to think about a lot of the women saying they have herpes," she added. ■

Valacyclovir Safe for Long-Term Suppression of Genital Herpes

BY SHARON WORCESTER
Southeast Bureau

CHARLESTON, S.C. — Once-daily treatment with valacyclovir for the suppression of genital herpes caused by herpes simplex virus type 2 was well tolerated for up to 20 months in a recent study.

Previously, data were available only for patients who used daily valacyclovir for up to 12 months, Zane A. Brown, M.D., of the University of Washington, Seattle, and his colleagues reported in a poster at the annual meeting of the Infectious Diseases Society for Obstetrics and Gynecology.

For the current study, which was supported by GlaxoSmithKline Inc., 1,484 serodiscordant, heterosexual, monogamous couples were enrolled, and the seropositive partner was randomized to receive either placebo or 500 mg/day of valacyclovir for 8 months. The results of this double-blind phase, which were previously reported by the investigators, showed that the treatment significantly reduced the risk of genital herpes transmission.

Following the double-blind phase, 1,018 of the 1,484 participants treated in the double-blind phase entered an open-label suppression phase of the study, which provided 12 months of suppressive therapy with 500 mg/day of valacyclovir. Patients in this phase were evaluated every 3 months for laboratory values and adverse events.

More than 85% of participants who completed the entire 20 months of treatment were at least 80% compliant with the study medication. During the double-blind and open-label phases, the nature and incidence of adverse events were similar in the 519 participants originally assigned to receive valacyclovir (treatment group) and the 499 originally assigned to receive placebo. Common adverse events included headache, nasopharyngitis, and upper respiratory tract infection.

The findings suggest that daily valacyclovir is as safe for up to 20 months as it is for 8-12 months.

DR. BROWN

Serious adverse events were reported infrequently and were similar in frequency in the treatment group (5% incidence rate) and the placebo group (3% incidence rate). Only one serious adverse event (gastritis in one patient) during the 20-month study was considered by the investigators to be possibly attributable to valacyclovir, and it occurred during the open-label portion of the study.

Adverse events leading to treatment discontinuation occurred in fewer than 1% of those in the treatment group, and in 1% of those in the placebo group; clinically significant laboratory abnormalities occurred in 6% of patients in both groups. No deaths occurred during the study periods.

Despite prior lack of data on the safety of valacyclovir for the suppression of genital herpes when used for longer than 12 months, some physicians prescribe such therapy for longer periods, the investigators noted. These findings suggest that the treatment is as safe for up to 20 months as it is with 8-12 months of suppressive therapy, they concluded. ■

HPV Testing May Help in Managing Cervical Lesions

BY SHERRY BOSCHERT
San Francisco Bureau

VANCOUVER, B.C. — Low-grade squamous intraepithelial lesions were likely to regress in women older than 30 years who were not infected with types of human papillomavirus associated with a high risk for cervical cancer, a longitudinal study found.

Of 412 women with untreated cervical low-grade squamous intraepithelial lesions (L-SIL), only women who tested positive for high-risk human papillomavirus (HPV) developed cervical intraepithelial neoplasia grades 2 or 3 (CIN 2/3) during 2 years of follow-up, Christine C. Clavel, Ph.D., said at the 22nd International Papillomavirus Conference.

HPV testing is approved in the United States to help triage women with Pap results showing atypical squamous cells of undetermined significance, or as an adjunct to Pap smears for screening women older than age 30. The study suggests that it also might be helpful by allowing a longer interval between follow-ups in women with L-SIL and a negative HPV test, said Dr. Clavel of the University of Reims (France) Hospital Center.

At baseline, 87% of the 412 women and 80% of those older than 35 years tested positive for high-risk HPV types. Colposcopy and biopsies found 21 cases of CIN 2/3 at baseline and an additional 12 cases during the 2-year follow-up, all in women who initially tested positive for high-risk HPV, she said at the conference, sponsored by the University of California, San Francisco.

Half of the high-risk HPV infections cleared over a median of 9 months in the cohort as a whole and in the subset of women older than 35 years. Cytologic lesions cleared over time in 66% of the total cohort and in 68% of women older than 35.

"There was a significant correlation observed between an initial negative high-risk HPV test, the regression of cytologic lesions, and the absence of CIN 2/3 in follow-up," Dr. Clavel said.

Women with L-SIL who test negative for high-risk HPV might safely be followed 12 months later by repeat cytology and HPV testing, she said. This would include approximately 13% of all women with L-SIL, 20% of these over age 35 with L-SIL, or 24% of women over age 45 with L-SIL. In women older than 45 years, misclassification of L-SIL increases and leads to a decrease in detection of L-SIL at colposcopy, she noted.

Using HPV testing plus Pap smears to follow HPV-negative women with L-SIL could significantly decrease the number of women sent to colposcopy, compared with follow-up using cytology alone, Dr. Clavel said. ■