

Check HIV Patients for Comorbid Herpes, Syphilis

BY HEIDI SPLETE
Senior Writer

WASHINGTON — Clinicians should be proactive in checking their HIV patients for herpes and syphilis because of the risk of coinfection, Dr. Connie Celum said at the Ryan White CARE Act meeting on HIV treatment.

"If you don't look for STDs in HIV patients, you won't find them," said Dr. Celum of the University of Washington, Seattle.

Individuals with STDs are two to five times more likely than those without STDs to become infected with HIV if they are exposed through sexual contact, according to data from the Centers for Disease Control and Prevention.

Comorbid STDs often go undetected in HIV patients, but an HIV-infected person who is coinfecting with an STD is more likely to transmit HIV than an HIV-infected person without a comorbid STD.

Genital herpes is the most common

sexually transmitted infection among HIV-positive persons, Dr. Celum said. Previous studies have shown that the herpes virus (HSV-2) increases one's risk of acquiring HIV and increases HIV RNA levels in plasma and in the genital tract; the presence of herpes also makes a person more likely to transmit HIV.

Conversely, the presence of HIV can reactivate herpes that has been dormant. HIV also increases the frequency of HSV-2 shedding in persons with herpes and in-

creases the risk of acquiring and transmitting the herpes virus. A recent study by Dr. Celum and her colleagues at the University of Washington found that 50 HIV-positive men with herpes were 2.7 times more likely to shed the herpes virus orally, compared with 59 HIV-negative men with herpes (*J. Infect. Dis.* 2006;194:420-7).

A key question is, if you suppress herpes, can you reduce the likelihood of HIV infection? Suppression of herpes may be a strategy that buys more time for researchers who continue to work on other HIV treatments and interventions, Dr. Celum said.

Data from a proof-of-concept study including 140 women coinfecting with HIV and herpes showed that treating herpes with valacyclovir significantly reduced HIV levels in plasma and the genital tract. The results were presented at the Conference on Retroviruses and Opportunistic Infections earlier this year, but useful clinical data are still 1-2 years away, she said.

The majority of herpes patients shed the virus in the genital tract. Although highly active antiretroviral treatment (HAART) may reduce symptoms of herpes, it does not reduce subclinical herpes shedding. Even if suppressing herpes infections with HAART can suppress the viral load in HIV patients, it remains to be seen whether treating herpes also reduces the likelihood of HIV infection.

Clinicians should also be vigilant in evaluating their HIV patients for syphilis because the annual incidence of syphilis is rising, especially among men who have sex with men, Dr. Celum explained.

The reasons for the resurgence of syphilis remain unclear, but some epidemiologic data suggest that improved therapy for HIV and improved survival and well-being among HIV patients may be driving the increase in cases, particularly among men who have sex with men. Most clinicians have limited experience in diagnosing syphilis, and they may not know it when they see it. Syphilis is a great imitator; the appearance of rashes and other signs of secondary syphilis vary from person to person.

Syphilis rashes may be widespread or subtle. The rashes are not usually itchy or vesicular, but they may include papules, macules, pustules, or ring- or lens-shaped lesions. A syphilis rash appears on the palms and soles in 60% of cases, not 100% of cases, so look elsewhere on the body for signs of infection after checking the palms and soles, Dr. Celum said. These symptoms usually appear after the chancres of primary syphilis have resolved. Syphilis manifestations are especially easy to miss in HIV-positive patients on HAART because these patients often develop rashes that resemble syphilis as a side effect of the medication.

Consequently, Dr. Celum recommends maintaining a high level of suspicion for syphilis in HIV-positive patients because of the increased risk of HIV transmission. She suggests treating for syphilis in possible as well as definite cases. ■

The most up-to-date treatment guidelines for syphilis and other STDs are available on the Centers for Disease Control and Prevention Web site at www.cdc.gov/std.

Plan B® (Levonorgestrel) Tablets, 0.75 mg

Brief Summary (See Package Brochure For Full Prescribing Information)

Rx only for women age 17 and younger

For women age 17 and younger, Plan B® is a prescription-only emergency contraceptive. Plan B® is intended to prevent pregnancy after known or suspected contraceptive failure or unprotected intercourse. Emergency contraceptive pills (like all oral contraceptives) do not protect against infection with HIV (the virus that causes AIDS) and other sexually transmitted diseases.

CONTRAINDICATIONS

Progestin-only contraceptive pills (POPs) are used as a routine method of birth control over longer periods of time, and are contraindicated in some conditions. It is not known whether these same conditions apply to the Plan B® regimen consisting of the emergency use of two progestin pills. POPs however, are not recommended for use in the following conditions:

- Known or suspected pregnancy
- Hypersensitivity to any component of the product

WARNINGS

Plan B® is not recommended for routine use as a contraceptive. Plan B® is not effective in terminating an existing pregnancy.

Effects on Menses

Menstrual bleeding patterns are often irregular among women using progestin-only oral contraceptives and in clinical studies of levonorgestrel for postcoital and emergency contraceptive use. Some women may experience spotting a few days after taking Plan B®. At the time of expected menses, approximately 75% of women using Plan B® had vaginal bleeding similar to their normal menses, 12-13% bled more than usual, and 12% bled less than usual. The majority of women (87%) had their next menstrual period at the expected time or within ± 7 days, while 13% had a delay of more than 7 days beyond the anticipated onset of menses. If there is a delay in the onset of menses beyond 1 week, the possibility of pregnancy should be considered.

Ectopic Pregnancy

Ectopic pregnancies account for approximately 2% of reported pregnancies (19.7 per 1,000 reported pregnancies). Up to 10% of pregnancies reported in clinical studies of routine use of progestin-only contraceptives are ectopic. A history of ectopic pregnancy need not be considered a contraindication to use of this emergency contraceptive method. Health providers, however, should be alert to the possibility of an ectopic pregnancy in women who become pregnant or complain of lower abdominal pain after taking Plan B®.

PRECAUTIONS

Pregnancy

Many studies have found no effects on fetal development associated with long-term use of contraceptive doses of oral progestins (POPs). The few studies of infant growth and development that have been conducted with POPs have not demonstrated significant adverse effects.

STD/HIV

Plan B®, like progestin-only contraceptives, does not protect against HIV infection (AIDS) and other sexually transmitted diseases.

Physical Examination and Follow-up

A physical examination is not required prior to prescribing Plan B®. A follow-up physical or pelvic examination, however, is recommended if there is any doubt concerning the general health or pregnancy status of any woman after taking Plan B®.

Carbohydrate Metabolism

The effects of Plan B® on carbohydrate metabolism are unknown. Some users of progestin-only oral contraceptives (POPs) may experience slight deterioration in glucose tolerance, with increases in plasma insulin; however, women with diabetes mellitus who use POPs do not generally experience changes in their insulin requirements. Nonetheless, diabetic women should be monitored while taking Plan B®.

Drug Interactions

Theoretically, the effectiveness of low-dose progestin-only pills is reduced by hepatic enzyme-inducing drugs such as the anticonvulsants phenytoin, carbamazepine, and barbiturates, and the antituberculosis drug rifampin. No significant interaction has been found with broad-

spectrum antibiotics. It is not known whether the efficacy of Plan B® would be affected by these or any other medications.

Nursing Mothers

Small amounts of progestin pass into the breast milk in women taking progestin-only pills for long-term contraception resulting in steroid levels in infant plasma of 1-6% of the levels of maternal plasma. However, no adverse effects due to progestin-only pills have been found on breastfeeding performance, either in the quality or quantity of the milk, or on the health, growth or development of the infant.

Pediatric Use

Safety and efficacy of progestin-only pills have been established in women of reproductive age for long-term contraception. Safety and efficacy are expected to be the same for postpubertal adolescents under the age of 16 and for users 16 years and older. Use of Plan B® emergency contraception before menarche is not indicated.

Fertility Following Discontinuation

The limited available data indicate a rapid return of normal ovulation and fertility following discontinuation of progestin-only pills for emergency contraception and long-term contraception.

ADVERSE REACTIONS

The most common adverse events in the clinical trial for women receiving Plan B® included nausea (23%), abdominal pain (18%), fatigue (17%), headache (17%), and menstrual changes. The table below shows those adverse events that occurred in $\geq 5\%$ of Plan B® users.

Table 3: Adverse Events in $\geq 5\%$ of Women, by % Frequency

Most Common Adverse Events	Plan B® Levonorgestrel N=977 (%)
Nausea	23.1
Abdominal Pain	17.6
Fatigue	16.9
Headache	16.8
Heavier Menstrual Bleeding	13.8
Lighter Menstrual Bleeding	12.5
Dizziness	11.2
Breast Tenderness	10.7
Other complaints	9.7
Vomiting	5.6
Diarrhea	5.0

Plan B® demonstrated a superior safety profile over the Yuzpe regimen for the following adverse events:

- Nausea: Occurred in 23% of women taking Plan B® (compared to 50% with Yuzpe)
- Vomiting: Occurred in 6% of women taking Plan B® (compared to 19% with Yuzpe)

DRUG ABUSE AND DEPENDENCE

There is no information about dependence associated with the use of Plan B®.

OVERDOSAGE

There are no data on overdosage of Plan B®, although the common adverse event of nausea and its associated vomiting may be anticipated.

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