Pre-exposure prophylaxis for the prevention of HIV infection: Ready for prime time

For prophylaxis to be effective, we must screen asymptomatic individuals during routine health encounters

Patrick Duff, MD

Dr. Duff is Professor of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, University of Florida College of Medicine, Gainesville.

The first cases of HIV infection in the United States were reported in 1981. Since that time, more than 700,000 individuals in our country have died of AIDS. Slightly more than 1 million persons in the United States are currently living with HIV infection; approximately 15% of them are unaware of their infection. Men who have sex with men (MSM) and African American and Hispanic/Latino men and women are disproportionately affected by HIV infection.[1] Among men, MSM is the most common method of infection transmission, accounting for 83% of infections. Heterosexual contact accounts for 9.4% of new infections and injection drug use for 4.0%. Among women in the United States, heterosexual contact is the most common mechanism of transmission, accounting for about 87% of cases; injection drug use accounts for about 12%.[1] Perinatal transmission rates are extremely low—less than 1%—when women receive effective treatment during pregnancy and their infants are treated in the neonatal period.[1,2]

The author reports no financial relationships relevant to this article.

The prognosis for HIV-infected patients has improved dramatically in recent years with the availability of many new and exceptionally effective highly-active antiretroviral treatment regimens. Nevertheless, the disease is not yet completely curable. Therefore, preventive measures are of great importance in reducing the enormous toll imposed by this condition.[2]

Evaluating effectiveness of PrEP

At the request of the US Preventive Services Task Force, Chou and colleagues recently conducted a systematic review to determine the effectiveness of pre-exposure prophylaxis (PrEP) in preventing the horizontal transmission of HIV infection.[1] The authors' secondary objectives included assessing the relationship between degree of adherence to the prophylactic regimen and degree of effectiveness and evaluating the accuracy of various screening systems for identifying patients at high risk for acquiring HIV infection.

The authors reviewed prospective, randomized controlled trials (treatment versus no treatment or treatment versus placebo) published through 2018. Pregnant women were excluded from the studies, as were women who became pregnant after enrollment.

Two different prophylactic regimens were used in the reviewed studies: 1) the combination of tenofovir disoproxil fumarate 300 mg or 245 mg plus emtricitabine 200 mg and 2) tenofovir 300 mg alone. Most trials used the combination regimen. With the exception of one trial, the medications were given daily to uninfected patients at high risk of acquiring HIV infection. In one investigation, the administration of prophylaxis was event driven (administered after a specific high-risk exposure).

Key study findings

PrEP decreased HIV transmission in high-risk patients. Chou and colleagues found that high-risk

CONTINUED ON PAGE 35

CONTINUED FROM PAGE 33

patients included primarily MSM who did not use condoms consistently or who had a high number of sex partners, individuals in an HIV-serodiscordant relationship, and intravenous drug users who shared injection equipment.

In these high-risk patients, PrEP was associated with a significantly decreased risk of HIV transmission. Observations from 11 trials demonstrated a relative risk (RR) of 0.46 (95% confidence interval [CI], 0.33–0.66). The absolute risk reduction was -2.0% (95% CI, -2.8% to -1.2%). The duration of follow up ranged from 4 months to 4 years.

Better medication adherence = greater prophylaxis effectiveness. When adherence was ≥70%, the RR was 0.27 (95% CI, 0.19–0.39). When adherence was 40% to 70%, the RR was 0.51 (95% CI, 0.38–0.70). When adherence was ≤40%, the relative risk was 0.93 (95% CI, 0.72–1.20). Adherence was better with daily administration, as opposed to event-driven administration.

Although the combination prophylactic regimen (tenofovir plus emtricitabine) was most frequently used in the clinical trials, tenofovir alone was comparable in effectiveness.

PrEP resulted in more mild adverse effects. Patients who received PrEP were more likely to develop gastrointestinal adverse effects and renal function abnormalities when compared with patients in the control arms of the studies. These adverse effects were virtually always mild and did not necessitate discontinuation of treatment.

No increase in promiscuous sexual behavior with PrEP. Specifically, investigators did not document an increased incidence of new sexually transmitted infections (STIs) in treated patients.

PrEP did not increase adverse pregnancy outcomes. In women who became pregnant while on PrEP, and who then discontinued treatment, there was no increase in the frequency of spontaneous abortion, congenital anomalies, or other adverse pregnancy outcomes.

In addition, PrEP posed a low risk for causing drug resistance in patients who became infected despite prophylaxis. Finally, the authors found that screening instruments for identifying patients at highest risk for acquiring HIV infection had low to modest sensitivity.

My recommendations for practice

Based on the study by Chou and colleagues, and on a recent commentary by Marcus et al, I believe that the following actions are justified[1–3]:

- For prophylaxis to be effective, we must identify all infected patients. Therefore, screening of asymptomatic individuals during routine health encounters is essential.
- All patients should have access to easy-to-understand information related to risk factors for HIV infection.
- Every effort should be made to promote safe sex practices, such as use of latex condoms, avoidance of sex during menses and in the presence of ulcerative genital lesions, and avoidance of use of contaminated drug-injection needles.
- All high-risk patients, as defined above, should be offered PrEP.
- To the greatest extent possible, financial barriers to PrEP should be eliminated.
- Patients receiving PrEP should be monitored for evidence of renal dysfunction. Should they become infected despite prophylaxis, they should be evaluated carefully to detect drug-resistant viral strains.
- Although PrEP is definitely effective in reducing the risk of transmission of HIV infection, it does not prevent the transmission of other STIs, such as syphilis, gonorrhea, and chlamydia.

In my practice, I administer prophyaxis on a daily basis rather than just before, or after, a high-risk exposure. This approach enhances patient adherence and, hopefully, will lead to maximum effectiveness over time. I also use the combination of tenofovir disoproxil fumarate plus emtricitabine rather than tenofovir alone because there is more published information regarding the effectiveness of the combination regimen. ●

References

1. Chou R, Evans C, Hoverman A, et al. Pre-exposure Prophylaxis for the Prevention of HIV Infection: A Systematic Review for the U.S. Preventive Services Task Force. AHRQ Publication No. 18-05247-EF-1; November 2018.
2. Duff P. Maternal and fetal infections. In: Resnik R, Lockwood CJ, Moore TR, Green MF, Copel JA, Silver RM (eds). *Creasy & Resnik's Maternal-Fetal Medicine. Principles and Practice (8th ed)*. Philadelphia, PA: Elsevier; 2019.
3. Marcus JL, Katz KA, Krakower DS, et al. Risk compensation and clinical decision making—the case of HIV preexposure prophylaxis. *N Engl J Med*. 2019;380:510-512.