Committee on Gynecologic Practice

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Preexposure Prophylaxis for the Prevention of Human Immunodeficiency Virus

ABSTRACT: Preexposure prophylaxis is defined as the administration of antiretroviral medications to individuals who are not infected with human immunodeficiency virus (HIV) and are at the highest risk of acquiring HIV infection. In combination with other proven HIV-prevention methods, preexposure prophylaxis may be a useful tool for women at the highest risk of HIV acquisition. Obstetrician–gynecologists involved in the care of women using preexposure prophylaxis must reinforce adherence to daily medication. The Centers for Disease Control and Prevention’s guidance for preexposure prophylaxis is likely to evolve in the coming years, and obstetrician–gynecologists should remain aware of new developments in this area. Risk reduction for all women at risk of HIV infection should include counseling about testing, safe-sex practices (including condom use), and other behavioral interventions.

Data From Clinical Trials

The use of daily tenofovir and emtricitabine was shown to be effective in decreasing HIV transmission in two prospective randomized trials of heterosexual men and women (4, 6); one trial found no effect (7) (see Table 1). Daily use of tenofovir and emtricitabine reduced the rate of new HIV infection by 62% in the trial of uninfected heterosexual men and women in Botswana (6). The second trial studied heterosexual discordant couples in Uganda and Kenya; in approximately one third of the study couples, the seronegative partner was female (4). Daily use of tenofovir and emtricitabine was 75% effective in decreasing transmission in this trial. Adherence to study medication, assessed with serum drug levels, pill counts, or self-reports, was high for both of these trials.

The third trial of tenofovir and emtricitabine studied heterosexual women in a variety of settings in Africa. In this trial, daily use of tenofovir and emtricitabine showed
no reduction in new HIV infections when compared with placebo; the authors hypothesized this was due to poor adherence to the study drug because only 15–25% of those who seroconverted had therapeutic serum levels of tenofovir (7, 8). No unusual adverse effects or safety concerns were noted among HIV-negative participants taking daily tenofovir and emtricitabine. The most common adverse effects included nausea and diarrhea, and these problems were frequently mild and resolved without treatment.

**Candidates for Preexposure Prophylaxis**

Women at the highest risk of acquiring HIV infection (eg, a woman not infected with HIV with a male sexual partner who is known to be infected with HIV) should be considered candidates for preexposure prophylaxis. Other potential candidates may include women who engage in sexual activity within a high HIV-prevalence area or social network and one or more of the following: inconsistent or no condom use; diagnosis of sexually transmitted infections; exchange of sex for commodities (such as money, shelter, food, or drugs); use of intravenous drugs or alcohol dependence or both; incarceration; or partner(s) of unknown HIV status with any of the factors previously listed (9). An abbreviated version of the interim CDC guidelines appears in Box 1. Risk reduction for all women at risk of HIV infection should include counseling about testing, safe-sex practices (including condom use), and other behavioral interventions.

The use of daily oral preexposure prophylaxis during pregnancy and lactation for women without HIV with HIV-infected partners has had limited study, and specifically was not addressed in the studies previously cited. The drug combination of tenofovir and emtricitabine is commonly used during pregnancy and has a reassuring safety profile. Human immunodeficiency virus infection is one of the few contraindications to breastfeeding (10), and clinicians should be vigilant for new HIV seroconversion in lactating women at risk of new HIV infection.

**Adherence Counseling and Other Interventions**

In the previously discussed preexposure prophylaxis clinical trials, adherence to study medication was the most important factor in reducing risk of HIV infection. Obstetrician–gynecologists involved in the care of women using preexposure prophylaxis must reinforce adherence to daily medication. In addition, safe-sex practices, especially consistent condom use, must be emphasized to maximize HIV prevention and prevent transmission of other sexually transmitted infections, and patients should be asked the reason they are not using condoms in order to assess whether the patient feels safe negotiating condom use. A combination of testing, education, and brief

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**Table 1. Clinical Trials of Preexposure Prophylaxis to Prevent Human Immunodeficiency Virus Transmission**

<table>
<thead>
<tr>
<th>Setting</th>
<th>Male (n)</th>
<th>Female (n)</th>
<th>Incidence rate of HIV infection per 100 person-years</th>
<th>Adherence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Botswana*</td>
<td>54.3% (662), 100%</td>
<td>45.7% (557), 100%</td>
<td>1.2 TDF-FTC versus</td>
<td>84.1% TDF-FTC versus</td>
</tr>
<tr>
<td></td>
<td>HIV-seronegative</td>
<td>HIV-seronegative</td>
<td>3.1 placebo</td>
<td>83.7% placebo†</td>
</tr>
<tr>
<td>Kenya and Uganda‡§</td>
<td>50% (4,747), 62%</td>
<td>50% (4,747), 38%</td>
<td>0.65 TDF versus</td>
<td>84% TDF versus</td>
</tr>
<tr>
<td></td>
<td>HIV-seronegative</td>
<td>HIV-seronegative</td>
<td>0.50 TDF-FTC versus</td>
<td>84% TDF-FTC versus</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1.99 placebo</td>
<td>85% placebo</td>
</tr>
<tr>
<td>Kenya, South Africa, and Tanzania¶</td>
<td>NA</td>
<td>100% (2,120), 100%</td>
<td>4.7 TDF-FTC versus</td>
<td>88% for both TDF-FTC</td>
</tr>
<tr>
<td></td>
<td>HIV-negative</td>
<td></td>
<td>5.0 placebo</td>
<td>and placebo*</td>
</tr>
</tbody>
</table>

Abbreviations: HIV, human immunodeficiency virus; NA, not applicable; TDF, tenofovir disoproxil fumarate; TDF-FTC, tenofovir disoproxil fumarate and emtricitabine.


†Adherence was calculated using pill count.


§ This trial included an arm of daily tenofovir, which also was effective as preexposure prophylaxis. However, tenofovir as a single agent is not currently approved by the U.S. Food and Drug Administration for preexposure prophylaxis.

|| Adherence was calculated using pill count, specifically bottles with 95% or more of doses taken.


Adherence was calculated using pill count. However, approximately 20–26% of women with HIV seroconversion had subtherapeutic drug levels in serum samples.
behavioral interventions can help reduce the rate of HIV infection and its complications.

Cost and Access

The success of preexposure prophylaxis for preventing HIV infection in U.S. women is tied to issues of cost and access. The average wholesale price for a standard dose of preexposure prophylaxis (300-mg of tenofovir and 200-mg of emtricitabine; one tablet daily) is estimated at $1,425 per month (11). Currently, no generic versions are available. Furthermore, the cost for the individual patient includes laboratory services and other professional fees (eg, follow-up visits and counseling for adherence and risk reduction), in addition to daily medication (11). To date, no private plan has publicly released its preexposure prophylaxis coverage policy and it is not covered by Medicaid or Medicare (11). A list of pharmaceutical company patient assistance programs and copayment assistance programs is available through the National Alliance of State and Territorial AIDS Directors (http://www.nastad.org/docs/PrEP%20and%20PEP%20PAP%20fact%20sheet.pdf).

Conclusion

In combination with other proven HIV-prevention methods, preexposure prophylaxis may be a useful tool for women at the highest risk of HIV acquisition. Adherence to prescribed prophylaxis may be the most critical variable in preventing HIV infection with preexposure prophylaxis. The CDC’s guidance for preexposure prophylaxis is likely to evolve in the coming years, and obstetrician–gynecologists should remain aware of new developments in this area. Any infection prevention strategy should include ongoing emphasis on safe-sex practices and risk reduction interventions.

Resources


References


