Hot News

Increased HIV Susceptibility and Transmissibility in Women Using Hormonal Contraception

Results from a prospective study of 3,790 HIV-serodiscordant heterosexual couples from seven countries in Sub-Saharan Africa have recently alerted about an increased risk of HIV acquisition using hormonal contraception (Heffron, et al. Lancet Infect Dis. 2012;12:19-26). The study was funded by the Bill & Melinda Gates Foundation. Among 1,314 HIV-seronegative women with an HIV-positive male partner followed for a median of 18 months, rates of HIV acquisition were nearly double in women who used hormonal contraception than in those who did not (6.6 vs. 3.8 per 100 person-years, respectively; $p = 0.03$).

On the other hand, among 2,476 couples in which the HIV-seronegative partner was the male, the rate of HIV transmission from infected women after a median follow-up of 18 months was again nearly double in those who used hormonal contraception than in those who did not (2.6 vs. 1.5 person-years, respectively; $p = 0.02$).

The association between hormonal contraception and risk of HIV acquisition and/or transmission was more pronounced in women who used injectable than oral hormones, highlighting a dose-dependent effect of hormones on the female genital tract that could make them more susceptible to HIV exposure if HIV-negative as well as more infectious if already HIV-positive. This study is important given the large size of the study populations and the relative long-term follow-up of couples. It provides robust evidence against the use of hormonal contraception in HIV-serodiscordant heterosexual partners in the absence of condoms.

Carmen de Mendoza
Infectious Diseases Department
Hospital Carlos III
Madrid, Spain

Tenofovir May Protect Against Herpes Simplex

The major message of the CAPRISA-004 trial (Abdool-Karim, et al. Science. 2010;329:1168-74), originally reported in July 2010, was that a vaginal microbicide gel containing 1% tenofovir could reduce the risk of HIV infection among promiscuous women by 39%.

The trial also showed a reduced incidence of herpes simplex virus (HSV)-2 by 51% in a subset of 450 women who were not already HSV-2 infected at the start of the trial. Now, researchers have reported a possible mechanism by which tenofovir inhibits HSV-2 (Andrei, et al. Cell Host Microbe. 2011;10:379-89). Experiments were performed testing the antiviral activity of 1% tenofovir gel in tissue samples taken from women infected with HSV-2. The concentration achieved intravaginally with the tenofovir gel had direct anti-herpetic activity, with inhibition of HSV-2 replication in cells found in epithelial or connective tissue from the female genital tract. A reduction in HSV-2 replication by as much as 99% in lymphoid and cervicovaginal tissue samples was recognized. In tissues from mice infected with HSV-2, 1% tenofovir gel also delayed the formation of lesions and even death. Researchers concluded that the active metabolite of tenofovir at high concentrations, as produced when using the topical gel, inhibited both HSV-2 DNA polymerase and HIV reverse transcriptase.

Pablo Barreiro
Infectious Diseases Department
Hospital Carlos III
Madrid, Spain

When to Start Antiretroviral Therapy in HIV Patients with Tuberculosis

Tuberculosis (TB) is the most common infectious cause of death in HIV-infected individuals worldwide. Although its incidence and severity increases as immunodeficiency worsens, TB may also appear in HIV-positive subjects with preserved CD4 counts. However, even in the last scenario, there is increased mortality of HIV-infected persons once TB has been diagnosed, regardless of CD4 counts. For this reason, current guidelines recommend initiation of antiretroviral therapy in all HIV/TB patients. However, early initiation of antiretroviral therapy, beginning either simultaneous with or soon after initiating TB drugs, may be associated with a lot of problems, including: (i) drug interactions; (ii) overlapping side effects; (iii) high pill burden and potential compromise in drug adherence; and (iv) immune reconstitution inflammatory syndrome (IRIS). Conversely, a delay in initiating antiretroviral therapy may result in the development of further opportunistic infections and premature death.

The results of three large studies (CAMELIA, ACTG A5221, and SAPIT) released in October 2011 (Blanc, et al. N Engl J Med. 2011;365:1471-81; Havlir, et al. N Engl J Med. 2011;365:1482-91; Abdool-Karim, et al. N Engl J Med. 2011;365:1492-501)

answered the question of when is the best time to initiate antiretroviral therapy in HIV-infected individuals presenting with TB. The results were uniform across all trials: initiation of antiretroviral therapy within two weeks of beginning TB treatment reduces mortality only in the subset of patients with low CD4 counts. However, this benefit comes at the expense of increased frequency of IRIS and drug-related adverse events. In HIV patients with > 200 $CD4^+$ T-cells/µl there was no difference in outcome when comparing groups with initiation of antiretroviral therapy before or after eight weeks of TB treatment. Therefore, it seems reasonable to defer initiation of antiretroviral therapy until the continuation phase of TB treatment in this population.

A major caveat in the message of these studies is that in HIV-infected patients with more severe TB forms, such as tuberculous meningitis, mortality rates are higher and intracranial IRIS could be fatal. In this regard, one study in Vietnam showed no reduction in mortality and increased frequency of severe adverse events in HIV patients with TB meningitis who began antiretroviral therapy within one week after diagnosis (Torok, et al. Clin Infect Dis. 2011;52:1374-83). In this specific situation, enough time of exposure to TB drugs should precede initiation of antiretroviral therapy to prevent further complications.

Pablo Labarga
Infectious Diseases Department
Hospital Carlos III
Madrid, Spain