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Hot News

Sexually Transmitted Infections on the Rise in PrEP Users

Pre-exposure prophylaxis (PrEP) with oral Truvada (tenofovir plus emtricitabine) is effective at preventing HIV infection in high-risk homosexual men. In the United States, PrEP was approved in 2012 and is reimbursed by Medicaid and the majority of private insurers. The situation is diverse and not uniform in the European Union, being PrEP more widely used in France than in the rest of countries.

Recent reports have alerted about a potential compensation risk effect among PrEP users, as result of loss of fear to acquire HIV, with sexual disinhibition, and engagement in riskier sexual practices, including anal sex, condomless use and with multiple partners, thereby increasing the chances of acquiring sexually transmitted infections (STIs). The impact of new tools and/or environments for making contacts, assisted by websites and apps *(websex)* may further contribute to increase exposures to distinct STIs (Duncan, et al. JMIR Mhealth Uhealth 2018;6:e10316). Lastly, the use of recreational drugs for enhancing sexual desire and extending sexual sessions (chemsex and slamsex), provides a further element for spreading in an unprecedented manner the chances for STI acquisition (Tomkins, et al. Perspect Public Health, in press).

High rates of STI have been reported among PrEP users, as well as high rates of condomless sex, and increasing rates of STI over time (Liu, et al. JAMA Intern Med. 2016;176:75-84; Kojima, et al. AIDS, 2016;30:2251-2). In a new study conducted in Montreal, Canada, increases in the rates of STI in PrEP users were demonstrated measuring incidence rates of STI before and following the initiation of PrEP in the same cohort. The authors measured the incidence of gonorrhea, chlamydia, and/or syphilis in 109 HIV-seronegative homosexual men 12 months before and 12 months after beginning Truvada for HIV prevention (Nguyen, et al. AIDS. 2018;32:523-30).

New episodes of gonorrhea, chlamydia, and/or syphilis rose in the cohort after providing Truvada, as shown in Figure 1. Moreover, the incidence of three or more STI increased from 3.7 to 9.2 cases per 100 person-years in this cohort.

The Canadian study highlighted that the rate of STI with PrEP was also higher than in a group of 86 homosexual men that had undergone PEP in Montreal during 2010–2015. Other findings of the study we the high rate of STI with anorectal location, symptomless STI (e.g., chlamydia) and the frequency of sex partners contacted by internet (Nguyen, et al. AIDS. 2018;32:523-30).

The increased rates of STI in PrEP users suggest a need to reinforce counseling and STI diagnosis and treatment efforts. Although PrEP may provide a public health benefit beyond the immediate prevention of HIV infection as result of bringing into care high-risk homosexual men who might not otherwise be seeking care for STI, doctors in charge must take this opportunity for informing adequately on STI and the risks inherent to multiple and occasional sexual contacts (Nguyen, et al. AIDS. 2018;32:523-30).

Pablo Barreiro
Carlos III-La Paz University Hospital
Madrid, Spain

Impact of Low-level Viremia on Treatment Outcomes During ART - Is it Time to Revise the Definition of Virological Failure?

The level of HIV-RNA in plasma (HIV viral load) is the main marker used to monitor the virological response to antiretroviral therapy (ART) in HIV-infected patients. The threshold used to define virological suppression has historically been dictated by the limits of detection of the commercial assays used to quantify the plasma viral load. Thus, as more sensitive assays have proliferated and become more widely available, the definition has shifted from < 400 cop/mL with the first generation assays, to < 50 cop/mL, to < 20 cop/mL currently. Thanks to the high efficacy of the new treatment combinations, most HIV treatment guidelines have since 2008 established that the goal of ART is to maintain virological suppression below < 50 cop/mL. However, some guidelines have continued to set the definition of virological failure as a confirmed plasma viral load > 200 cop/mL, or even > 1000 cop/mL according to the WHO guidelines for low-income and middle-income

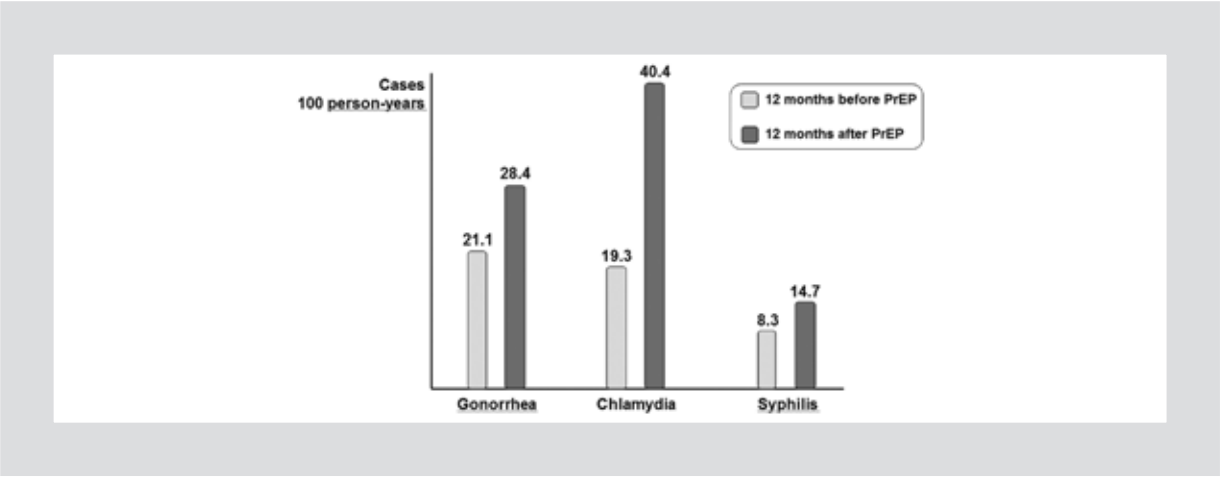

Figure 1. *Incidence of sexually transmitted infections before and after pre-exposure prophylaxis.*

countries. Several studies have evaluated the impact of low-level viremia as intermittent episodes (blips) or persistent detectable low-level viremia (50–1000 cop/mL) on treatment outcomes during ART. Some of these studies have suggested a potential role for low-level viremia as a predictor of virological failure, although up to now the data have been insufficient and controversial to guide clinical management.

Hermans et al. have recently published the results of a large (n = 70.930 HIV-infected patients) multicenter study (57 clinical sites in South Africa) with a median follow-up for more than 2 years, to evaluate the incidence and impact of low-level viremia (defined as HIV-RNA viral load of 51–999 cop/mL) and its association with virological failure (Hermans et al., Lancet Infect Dis 2018;18:188-97). This large cohort study concludes that overall, patients with low-level viremia are predisposed to subsequent virological failure. The risk of virological failure was 5 times higher for patients with low-level viremia ranging 400-999 cop/mL, and 2 times higher for those with viremia ranging 51–199 cop/mL, compared with patients maintaining viral load suppression (< 50 cop/mL). Interestingly, the risk of virological failure was significantly increased even after a single measurement of low-range low-level viremia ranging 51–199 cop/mL. Selection bias is a potential limitation of this study, mainly due to the inherent heterogeneity in the clinical management and treatment strategies among the 57 participating clinics. Despite this, the large sample size has allowed for performing a very detailed statistical analysis demonstrating the robustness of their conclusions.

The results of this large-scale study strongly suggest that low-level viremia should be considered as a warning signal for subsequent virological failure. Given these findings, therefore, the relevance of low-level viremia in the treatment outcomes for HIV-infected patients on ART should be recognized and considered in clinical decision-making. Furthermore, current WHO guidelines for low-income and middle-income countries should be revised and updated. Although substantial differences exist in the clinical management and treatment options between HIV-infected patients in high-income countries compared with low-income and middle-income countries, the results of this study call for the revision of the current definition of virological failure as a confirmed viral load of > 200 cop/mL established for most current HIV treatment guidelines. The implementation of new recommendations for the management of low-level viremia may have a huge impact in controlling the HIV epidemic. In the current era of increased efforts toward ending the HIV epidemic, all strategies are needed to help in finally achieving this much-needed objective.

Eva Poveda[1] and Manuel Crespo[2]
[1]Galicia Sur Health Research Institute (IIS Galicia Sur), Complexo Hospitalario Universitario de Vigo, SERGAS-UVigo, Spain
[2]Infectious Diseases Unit, Department of Internal Medicine, Complexo Hospitalario Universitario de Vigo, IIS Galicia Sur, SERGAS-UVigo, Spain