Pre-exposure prophylaxis in HIV

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1) Pre-exposure prophylaxis in HIV--a vision or soon a reality?

Reuter S, Meyer D, Knechten H, Oette M, Mitrenga D, Rockstroh J, Fätkenheuer G, Häussinger D. Pre-exposure prophylaxis in HIV--a vision or soon a reality? Dtsch Med Wochenschr. 2009;134:2582-4.

Condom use is propagated as the most efficient measure to prevent human immunodeficiency virus (HIV) transmission. For several reasons condoms are NOT ALWAYS used or misapplied during sexual intercourse. Therefore, alternative preventive measures through intake of antiretroviral drugs before sexual intercourse with an (presumably) HIV-positive person are being considered, thus called pre-exposure prophylaxis (PrEP). In animal models, the efficacy of HIV-PrEP was shown for Tenofovir alone or in combination with Emtricitabine. Several clinical studies are currently being conducted in different HIV risk groups in various continents. First results from these studies are anticipated for the year 2010. In case of proven efficacy for HIV-PrEP, our health system would face a large interdisciplinary challenge. It would be a difficult task to define the appropriate recipients. Measures would have to be taken to limit possible misuse of antiretroviral drugs due to the negative consequences with development of resistance, adverse events and illegal trading. It is already evident that HIV-PrEP will not provide absolute protection nor will it replace other preventive strategies. However, if used cautiously, HIV-PrEP might be established as a useful supplement in the prevention of HIV. Paramount questions from the fields of epidemiology, behavioral science, logistics, health politics and ethics should be answered in advance.

2) HIV preexposure prophylaxis in the United States: Impact on lifetime infection risk, clinical outcomes, and cost effectiveness.

Paltiel AD, Freedberg KA, Scott CA, Schackman BR, Losina E, Wang B, *et al*. HIV preexposure prophylaxis in the United States: Impact on lifetime infection risk, clinical outcomes, and cost effectiveness. Clin Infect Dis 2009;48:806–15.

The combination of Tenofovir and Emtricitabine shows promise as HIV-PrEP. In a cohort with a mean age of 34 years, PrEP reduced the lifetime HIV infection risk from 44% to 25% and increased the mean life expectancy from 39.9 years to 40.7 years (21.7–22.2 discounted quality-adjusted life-years). Markedly larger reductions in lifetime infection risk (from 44% to 6%) were observed with the assumption of greater (90%) PrEP efficacy. More favorable incremental cost-effectiveness ratios were obtained by targeting younger populations with a higher incidence of infection and by improvements in the efficacy and cost of PrEP.

PrEP could substantially reduce the incidence of HIV transmission in populations at high risk of HIV infection in the United States. Although it is unlikely to confer sufficient benefits to justify the current costs of Tenofovir emtricitabine, price reductions and/or increases in efficacy could make PrEP a cost-effective option in younger populations or populations at a higher risk of infection. Given recent disappointments in HIV infection prevention and vaccine development, additional study of PrEP-based HIV prevention is warranted.

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3) Pre-exposure prophylaxis and timed intercourse for HIV-discordant couples willing to conceive a child.

Vernazza P, Brenner I, Graf I. Cantonal Hospital St. Gallen, Switzerland. AIDS: 2008;22:647-8.

The true number of HIV-discordant couples who practice unprotected sex to conceive is most likely underestimated. The risk of transmission in a couple with a fully treated male partner is low and can further be reduced by timed intercourse and a short pre-exposure prophylaxis with Tenofovir. The pregnancy rates of natural conception are substantially higher than that with artificial reproduction techniques (40% in our program).

Twenty-one couples decided to use the proposed risk-reduction strategy with timed intercourse and Tenofovir disoproxil fumarate (TDF)-pre-exposure-prophylaxis. All male partners were subjected to a fully suppressive antiretroviral treatment. All women were negative for HIV. Six couples admitted that they had previously tried to conceive by unprotected intercourse. Eleven of 21 female partners conceived after three cycles. Fifteen of 21 female partners got pregnant after up to 10 attempts. All women tested negative for HIV-antibodies 3 months after the last exposure.

4) Antiretroviral pre-exposure prophylaxis (PrEP) for preventing HIV in high-risk individuals.

Okwundu CI, Okoromah CA. Antiretroviral pre-exposure prophylaxis (PrEP) for preventing HIV in high-risk individuals. Cochrane Database Syst Rev 2009;1:CD007189.

This review evaluated the effects of antiretroviral PrEP for preventing HIV infection in high-risk individuals. We identified 10 trials; eight ongoing or planned and two completed. Only one of the two completed trials met the criteria for this review. It was found that daily oral use of TDF in HIV-uninfected women was not associated with increased adverse events. The effectiveness of TDF in reducing the risk of acquiring HIV could not be evaluated conclusively because of the small number of HIV infections observed during the trial. The result, however, provides a rationale for further clinical trials to measure the value of oral antiretroviral drugs as prophylaxis against HIV infection. As a new approach to HIV prevention, prophylactic use of TDF or any other antiretroviral drug cannot be recommended at present. Larger clinical trials are needed to determine the effectiveness and safety of using any drug for PrEP against HIV infection in various risk groups.

5) The paradox of pre-exposure prophylaxis: Effects on incidence and transmitted resistance in San Francisco.

Supervie V, García-Lerma G, Heneine W, Blower S. Semel Inst for Neurosci and Human Behavior, David Geffen Sch of Med, Univ of California, Los Angeles, US and CDC, Atlanta, GA, US.**Plz provide complete details**

The administration of PrEP has gained considerable attention as a potential biomedical intervention to protect high-risk HIV people against infection. Several efficacy trials of daily PrEP with Tenofovir (TDF) alone or with Emtricitabine (FTC) are now ongoing among high-risk populations. A major concern is that drug resistance may develop in persons who fail PrEP or if PrEP is used by HIV-infected individuals.

We predict that PrEP, if used by 70% (median) of males who have sex with males (MSM), having a median efficacy of 60%, could increase transmitted drug resistance (TDR) from 10 to a median of 31% while preventing ~58% (median) of HIV infections over the next 10 years in San Francisco. Paradoxically, we find that increasing PrEP efficacy increases both the number of infections prevented and the proportion of cases of TDR thus increasing the number of infections with drug-resistant strains. Our results imply that it will be essential to develop new PrEP regimens with increased efficacy against drug-resistant strains.

EDITORIAL COMMENT

With an effective vaccine years away and microbicides still not available, there is mounting evidence that antiretroviral agents may be able to play an important role in reducing the risk for transmission. PrEP could provide an additional safety net for all men and women at risk due to sexual or drug-using behaviors when combined with reducing the number of sexual partners, HIV counseling and testing, condom use, use of sterile syringes and other prevention measures.

But, it should be remembered that, it is just a protection measure against HIV infection and not other sexually transmitted infections (STI). There may be viral STI that are asymptomatic, but viral shedding occurs and causes viral infection. Also, the risk of transmitting viral STI is greater in HIV-infected patients. Ultimately, PrEP is not a substitute to the barrier method; it is just a supplementation.