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EDITORIAL ARTICLE

THE EFFECT OF EMTRICITABINE AND TENOFOVIR USE IN THE PRE-EXPOSURE PROFYLAXIS (PrEP) FOR HIV TRANSMISSION

Over the past few decades, the introduction and growing use of emtricitabine and tenofovir (FTC / TDF) has represented a major advance in the management of sexually transmitted infections such as Human Immunodeficiency Virus (HIV), Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) infections.[1]

Emtricitabine (FTC) is a synthetic nucleoside analogue of cytidine with specific activity against HIV-1, HIV-2 and HBV. It competitively inhibits HIV-1 reverse transcriptase resulting in the termination of DNA chain synthesis. Also, emtricitabine is a weak inhibitor of mammalian α, β and ε DNA polymerases and mitochondrial DNA polymerase gamma.[1]

Tenofovir (TDF) inhibits HIV-1 reverse transcriptase and HBV polymerase by direct competitive binding to the natural deoxyribonucleotide substrate as well as by terminating DNA chain synthesis after its incorporation into DNA.[1]

HIV is an RNA-virus, which belongs to the retrovirus family and affects mainly macrophages and T-helper lymphocytes (CD4+). It is transmitted through sexual contact, hematogenously and vertically from mother to child during pregnancy, childbirth or breastfeeding.[1]

We conducted a literature review to examine the efficacy of the combination of emtricitabine and tenofovir in sexually transmitted infections, such as HIV, HBV and HCV. We particularly focused on the efficacy of the combination of emtricitabine and tenofovir in HIV infection.

Eight studies enrolling a total of 32,395 participants were selected, comparing emtricitabine / tenofovir to placebo, tenofovir per os, tenofovir in vaginal gel before or / and after sexual activity. The overall protective efficacy of daily FTC / TDF prophylaxis was 62.2% (95% CI, 21.5 to 83.4; P=0.03). There was no statistically significant difference between the combination of FTC / TDF and TDF monotherapy in men, women and couples.

According to a study by Grant et al, 2010, in 2,499 MSM (Men Sex with Men) and TGW (Trans Gender Women), the protective effect of FTC / TDF was compared to that of placebo. 10 were found to be infected with HIV at enrollment and 100 became infected during follow-up (36 in the FTC / TDF group and 64 in the placebo group), indicating a 44% reduction in the incidence of HIV (95% CI 15-63; p=0.005).[2]

According to the study by Thigpen et al, 2012, in a total of 1,219 male and female participants, daily FTC / TDF prophylaxis prevented HIV infection. The overall protective efficacy of FTC / TDF was 62.2% (95% CI, 21.5 to 83.4; P=0.03).[3]

In the study of Baeten et al, 2012, in a total of 4,758 couples, the protective effect of FTC / TDF was compared to that of TDF. No statistically significant difference was found between the two groups (P=0.23). Both regimens reduced HIV infections in men and women with comparable efficacy.[4]

In the study of Murnane et al, 2013, out of a total of 4,733 male and female participants, including subgroups of women with a high incidence of HIV-1 infection, the protective effect of FTC / TDF was compared to that of TDF. The overall incidence of HIV-1 in the placebo arm was 2.0 per 100 person-years and Pre-Exposure Prophylaxis (PrEP) efficacy was 67%

(95% CI 41-81, p<0.001) for TDF and 75% (95% CI 55-87, p<0.001) for FTC / TDF. Among women enrolled, overall HIV-1 incidence in the placebo arm was 2.8 per 100 person-years, TDF efficacy was 71% (95% CI 37-87, p=0.002) and FTC / TDF efficacy was 66% (95% CI 28-82, p=0.05). Among higher-risk subgroups PrEP (FTC / TDF and TDF) was protective against acquisition of HIV-1 with an efficacy ranging from 64% to 84%.[5]

Another study by Baeten et al, 2014, in a total of 4,410 couples, showed that plasma TDF detection levels correlated with a relative risk reduction in HIV-1 acquisition from 85%-93%, depending on whether they received TDF or FTC / TDF respectively (P<0.0001 in both groups). Prevention efficacy for HIV-1 infection was not statistically significant in both groups (P=0.16).[6]

The results of a study by Molina et al, 2015, out of a total of 414 MSM participants, 400 individuals who had no HIV infection were enrolled (199 in the FTC / TDF group and 201 in the placebo group). All participants were followed for an average of 9.3 months. A total of 16 HIV-1 infections occurred during follow-up, 2 in the FTC / TDF group and 14 in the placebo group. The relative reduction in the FTC / TDF group is 86% (95% CI 40 to 98; p=0.002).[7]

McCormack et al, 2015, a total of 544 MSM participants were randomly assigned to receive daily combined emtricitabine / tenofovir either immediately or after a period of 1 year. Three HIV infections occurred in the immediate group versus 20 in the second group despite 174 prescriptions of post exposure prophylaxis in the second group (relative reduction 86%, 90% CI 64-96, p=0.0001).[8]

Finally, in the study of Marazzo et al, 2015, in 5,029 women of childbearing age the protective effect of FTC / TDF was compared to that of TDF and TDF gel. Out of the 312 seroconversions included in the primary analysis, 52 occurred in the TDF group, 61 in the FTC / TDF group, 61 in the TDF gel group, 60 in the oral placebo group and 70 in the placebo gel group. The effectiveness was -49.0% with TDF (hazard ratio for infection, 1.49; 95% CI, 0.97 to 2.29), -4.4% with FTC / TDF (hazard ratio 1.04; 95% CI 0.73 to 1.49) and -14.5% with TDF gel (hazard ratio, 0.85; 95% CI, 0.61 to 1.21). There was no significant difference in the rate of HIV-1 seroconversion between the group receiving any study product and the group receiving the corresponding placebo, and the incidence of HIV-1 seroconversion did not change significantly during the study.

Consequently, the use of emtricitabine and tenofovir is more effective in preventing transmission of HIV compared to placebo or other combinations. The protective effect of FTC / TDF compared to TDF monotherapy was not statistically significant.

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