The role of drugs in HIV prevention

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Abstract. WHO reports 36.7 million people are living with Human Immunodeficiency Virus (HIV) worldwide by 2016 with about 1.8 million new infections each year. It will be a specific health problem for the world in both developed and developing countries so it is necessary strategies to reduce HIV transmission to the community. HIV transmission in people with risk factors is largely determined by the amount of virus in the blood of people who are the source of infection. Antiretroviral (ARV) therapy has long been used in HIV patients, which serves to suppress viral replication so that the patient's immunity increases; opportunistic infections are resolved and prolong the lifespan and lower transmission rates. In the HIV Prevention Trials Network (HPTN) study 052 there was a 96% reduction in transmission in earlier antiretroviral. ARV is also used in the prevention of transmission in people exposed to HIV virus that is Post-exposure Prophylaxis as well as in people at risk before exposure (Pre-exposure Prophylaxis). Three prevention strategies with the provision of ARV is expected to be guided as a means of prevention of transmission in addition to behavioral changes has long been declared since the beginning of the HIV epidemic.

1. Introduction

WHO estimates 36.7 million people are living with Human Immunodeficiency Virus (HIV) in the world by 2016 and about 1.8 million new infections will occur each year, 1 million have deaths.[1] This will be a major health problem in the world in both developed and developing countries. Various ways to prevent transmission through behavior change have been advocated such as abstinence, loyalty to couples and condom use but have little impact on reduced transmission of HIV. This is because of those who have a high risk of HIV transmission does not consistently implement it.[2]

Antiretroviral (ARV) has long been used for the treatment of HIV infection whereas antiretroviral drugs suppress viral replication so that the number of viruses decreases in the blood. 6-month antiretroviral treatment can reduce the HIV virus count <500 copies/ml by 53-83%.[3] If the HIV virus number of fewer than 1500 copies/ml of HIV transmission is rare, viral load is a major predictor of heterosexual transmission risk.[4] If the amount of virus in the blood decreases will cause the amount of virus in the semen, vaginal and rectal fluid also decreases.[5]

Pregnant women given antiretroviral drugs can reduce their transmission to below 1%.[6] In a study of HTPN 052 where the study was conducted on heterosexuals with serodiscordant couples in which most participants had vaginal intercourse, HIV transmission was reduced by 96%.[7] Seeing the results of this study provides hope for the prevention of HIV transmission by the provision of antiretroviral drugs. At present, some countries recommend the provision of antiretroviral drugs as

soon as thediagnosis of HIV infection is enforced (Test and Threat) like theUSA.[8] In Indonesia alone implement the strategic use of antiretroviral (SUFA) to achieve three zeros proclaimed by the government of zero new infection, zero AIDS-related death and zero discrimination.[9]

Research on Macaqua given exposure to HIV virus then given antiretroviral drugs can prevent transmission of post-exposure prophylaxis.[10] At the time of conducting health care workers can experience the process of exposure through a needle puncture that has been used HIV patients, exposed to blood to the mucosa or wounded skin. For such cases, an ARV is given to prevent transmission called Post Exposure Prophylaxis (PEP).

Recently, antiretroviral drugs are the therapy to people at risk of becoming infected with HIV before the person has an infection called prophylactic pre-exposure (PREP). PREP is a promising new approach to HIV prevention.[11] Based on the above exposure we would like to convey how the role of ARV drugs in the prevention of transmitting HIV.

2. Treatment as prevention

In a study in Rakai, Uganda the first empirical data on viral suppression by ARVs could decrease sexually transmitted HIV in serodiscordant partners [4] Cohen et al. In the HIV Prevention Trials Network (HPTN) study 052 comparing antiretroviral treatment in HIV-positive couples serodiscordant. The study consisted of 2 first groups with CD4 counts between 350-550 cells per millimeter per cubic and the second group with CD4 count <250 cells per cubic millimeter.

The rate of transmission decreased by 96% in the earlier antiretroviral group.[7] Several cohort studies on a man who has sex with a man (MSM) given antiretroviral therapy (ART) showed a lower risk of HIV transmission in couples. It is similar to be obtained in heterosexuals [12] at partner. The study showed no partner transmission during follow-up when viral load <200 copies/ml, were in this study 67% of heterosexual couples and 33% of couples were homosexual.[13]

Research on people who inject drugs (PWID) in Canada as a population, gave antiretroviral guideline given at symptomatic patient regardless of CD4 levels and in asymptomatic patients when CD4 <500 cells/ml. They found a decrease in HIV diagnostic rates, increasing rates of testing, ART coverage and viral suppression.[4]

The antiretroviral drugs administered to pregnant women when the anterior partum, intrapartum and the newborn baby for six weeks were shown to decrease 2/3 of transmission rates in their infants.[15] HIV positive mothers are less likely to transmit if their viral load is less than 1000 copies/ml.[16] Highly Antiretroviral Treatment given to HIV positive pregnant women for prevention mother to child transmission may reduce transmission to 1%.[6]

WHO recommendations on PMTCT regimens change year by year in which antiretroviral therapy is administered at a given gestational age until the baby is born but since 2013 ARVs are a therapy to Pregnant women (PW) / breastfeeding (BF) as a treatment for their health and prevention of their infants.[17]

WHO guidelines (2013) recommend Antiretroviral treatment regardless of CD4 count or clinical stage when HIV-positive patients have serodiscordant partners.[17] In the USA and France imposed a Test and Treat policy for HIV positive patients.[18] In Indonesia with the SUFA strategy, antiretrovirals are provided to all populations and specific groups with HIV positive. The key populations are Sex workers, MSM, IDU's, transvestites, while special groups include pregnant women, hepatitis patients, tuberculosis patients, serodiscordant couples, STIs, and prisoners.[9]

3. Post-exposure prophylaxis

Dendritic cells in the mucosa and skin are the initial target of the HIV. In primates, the first 24 hours of HIV infection is present in the dendritic cells and within 24-48 hours then move towards the regional lymph nodes and infect the lymphocytes there. It will be in the blood of the peripheral after 5 days of inoculation.[10]

Animal studies have shown that PEP is administered within 24 hours and continued for up to 28 days no infected animals. This finding is the basis of PEP delivery to people exposed to the HIV. PEP

is administered both to occupational and non-occupational exposure. At occupational exposure it is usually high exposure to percutaneous and exposures when the injury by needle perforation, the injury is deep, the source of exposure is an advanced HIV patient and encountered with blood on the surface of the tool. The rate of transmission through percutaneous inoculation is 0.3%.

In non-occupational exposures, it is usually through sexual intercourse that the highest risk of recipients is receptive anal intercourse followed by insertive anal intercourse and receptive vaginal intercourse then insertive vaginal intercourse. Assessment of the source of exposure is also indispensable whether the source of HIV-positive exposure has a high viral load e.g., patient with acute seroconversion, chronic infection with viral load> 1500 copies/ml.[20]

When PEP is best treated, PEP should be given as soon as possible, within hours of exposure.[10] Research on macaques shows better benefit when PEP administered under 24 hours post-exposure versus 72 hours post exposure. Giving PEP is indicated in percutaneous exposure, mucosal and non-intact skin exposure, unprotected sex, protected sex with condom failure, wound exposure, intravenous drugs user (IDU's).[10]

The regiment for PEP differs from country to country. CDC 2013 recommends Tenofovirdisoproxilfumarate (TDF) + emtricitabine (FTC) combined with raltegravir. Alternative options two nucleoside reverse transcriptase inhibitors (NRTIs) and integrase inhibitors, a ritonavir-boosted protease inhibitor or non-nucleoside reverse transcriptase (NNRTI).[10]

WHO recommends TDF + FTC / 3TC in combination with ritonavir/Lopinavir or either RAL, DRV / r or EFV. PEP feeds are at least 72 hours post-exposure or faster and given up to 28 days (21). Antiretroviral is not a recommendation as PEP between other, didanosine, nelfinavir, tipranavir. The viral antiretroviral is acontraindication for PEP is nevirapine.[10]

4. Pre-exposure prophylaxis

Antiretroviral given for Pre Exposure Prophylaxis may decrease the rate of transmission of HIV infection. Malina et al studied by giving the ARV pre-exposure on MSM using TDF + FTC with the PrEP driven event method and proven to decrease the rate of transmission by 86%.[22]

No difference in the TDF + FTC protective effect administered daily on PrEP [11] studies only lower pill requirements in those using PrEP with the event-driven method. CDC in 2014 recommends giving TDF to IDU's and active heterosexuals as alternative regimens.[23] There is a study that gives TDF vaginal gel 1% to effectively reduce transmission by 39%.[24]

Various clinical studies have been undertaken to determine the effectiveness of PrEP in HIV-infected high-risk patients. Research targets are also diverse in both adult heterosexual MSM, heterosexual serodiscordant, high-risk women, IDU's and women of reproductive age. ARV used in this study TDF or TDF + FTC. The protective effect of PrEP also varies from low to high even up to 86% and this protective effect is strongly associated with good adherence. The protective effect is higher when adherence is above 80%.[2]

Marcus JL et al found that no HIV seroconversions occurred duringPrEP use; where 92% adherence.[25] Some studies use other drugs as PrEP drugs. Maraviroc did not show a protective effect on PrEP.[11] A study using dapivirine showed dapivirine ring reduced the risk of HIV infection by 27 percent in women study population overall and 61 % of Population of 25 years or up provided no statistically significant protection in women younger than 25 years.[26]

Cabotegravir injection that has long-term effects seems promising, currently still under study [11] The use of antiretroviral drugs in PrEP also has side effects but is not found seriously only grade 1 and grade 2 in the form of impaired liver, kidney function, gastrointestinal disorders, decreased bone mass where this disorder will recover after the drug is stopped. The drugs used in PrEP are TDF and TDF + FTC. ARV resistance is also found in some studies but is very rare.[2]

5. Comparison of USA, Europe, WHO and Indonesia guideline

Various guidelines have implemented antiretroviral treatment as prevention of HIV transmission, The International AntiviralSociety-USA Pane recommends that antiretroviralis given to HIV infected

patients with detectable viremia regardless of CD4 cell count, Recommended Initial regimens: - Integrase Inhibitor (InSTI) + 2 Nucleoside Reverse Transcriptase Inhibitor.

Guidelines British HIV Association (UK) 2016 recommends the provision of ARVs to all HIV infected patients, with regimen 2 Nucleoside reverse transcriptase + boosted PI or NNRTI or InSTI.

Similarly, the WHO guideline of 2016 recommends the provision of ARVs to HIV infected patients primarily prioritized among all adults with severe or advanced HIV clinical disease (WHO clinical stage 3 or 4) and adults with CD4 count <350 cells / mm3, with TDF + 3TC regimens (orFTC) + EFV.

Indonesian Health Ministry recommends the provision of ARVs toHIV Infected patients with CD4 cell count <350 / mm3, key population, TB co-infection, Hep B co-infection, Pregnant / Breastfeeding woman, serodiscordant couple, HIV positive patients in hight epidemic region with regiment TDF + 3TC / FTC + EVF.

Giving ARV to Pre-Exposure Both USA, UK and WHO guidelines recommend the administration of Tenofovir / Emtricitabine (TDF / FTC) given daily or intermittently before sexual intercourse while the Indonesian Health Ministry does not allow until now.

For Post-exposure Prophylaxis, all guidelines recommend with different regiments. UAE guideline recommends TDF / FTC + Raltegravir or dolutegravir, UK guidelines TDF / FTC + Raltegravir.WHO guideline recommends TDF + 3TC / FTC + LPV / r OR ATV / r, Ministry with TDF + 3TC / FTC + LPV / r. Looking at the existing guidelines, all recommend ARVs as soon as possible and also recommend the provision of Post-Exposure Prophylaxis and later Pre Exposure Prophylaxis, it seems that all countries are committed to stopping the HIV epidemic.

6. Conclusion

1) Transmission of HIV infection is closely related to the amount ofvirus present in the blood of the sick person.
2) So that the provision of antiretroviral that can dramatically decrease and prevent the amount of virus transmitted in the blood.
3) Using ARV as aprecaution can be a Treatment Post Exposure Prophylaxis and also Pre-Exposure Prophylaxis.

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