The use of option B+ in prevention of mother to child transmission of HIV infection programs

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BACKGROUND

The idea of 'Option B+' is first put into practice by the Ministry of Health of Malawi, as CD4 testing for all human immunodeficiency virus (HIV)+ pregnant ladies was not possible there to kick-start the process of universal prevention of mother to child transmission (PMTCT). Though a baseline CD4 count is very important to diagnose immunologic failure after years, as long as viral load count is not universally available.[1]

The main argument in favor of using the option (in place of option B) to the local authority is that 'no study has shown intermittent therapy (starting and stopping of antiretrovial therapy (ART) in a healthy young lady) is beneficial for the HIV client at any stage of the disease'. And the other point to convince the authority about 5 years ago was that 'more and more studies were proving beneficial in starting ART at a higher CD4 count than before'.

Though the challenges described here are specific to Malawi, but these are also common in most of the developing world, particularly in sub-Saharan African setting.

BENEFITS TO THE CHILD

The expansion of the PMTCT program in Malawi through implementation of option B+ would have various other benefits. The total fertility rate in Malawi is high, around five to six births per woman, which is unlikely to be much lower in HIV-infected women. Soon after the breastfeeding period (median duration 23 months) many women become pregnant again. Thus, a stop-start approach to ART administration is almost redundant. Many women present for antenatal care late in pregnancy—an estimated 50% are thought to attend after 28 weeks of gestation—and continuing prophylaxis with antiretroviral drugs would mean that the next pregnancy could be protected from conception. The stopping of ART after cessation of breastfeeding might lead to viral rebound, with the risk of transmission to a sexual partner or fetus being notably raised.

In women in Zimbabwe even those with CD4 cell counts higher than 350 cells per μL had a risk of death around six times higher than that in noninfected women within 24 months post-partum[2,3], and early ART could reduce mortality by 50-90%.[4] Prevention of maternal deaths has a striking effect on child survival, independent of any effect gained from the prevention of HIV transmission.

The infant needs to take nevirapine or zidovudine from birth through age 4-6 weeks regardless of infant feeding method, which is quite straightforward to follow by the healthcare workers in the field as well as the naïve mothers.

Universal, lifelong ART for HIV-infected pregnant women will achieve maximum coverage and could potentially lead to elimination of pediatric HIV/acquired immunodeficiency syndrome (AIDS).

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BENEFITS TO THE MOTHER

Scheduled stopping is also difficult to implement, as it requires tapering of doses to prevent drug resistance, owing to the different half-lives of the antiretroviral drugs. Additionally, the risks of opportunistic disease or death might be raised. Tenofovir and lamividine are active against hepatitis B virus;[5] 10-15% of people living with HIV infection in Malawi are also infected with hepatitis B virus,[6] and reactivation of this virus is a risk if ART is stopped.

The risk of developing tuberculosis increases with declining CD4 cell counts, from 500 cells per μL;[7] the majority of pregnant women have CD4 cell counts in this range. Early initiation of ART,[8] therefore, reduces the risk of tuberculosis. Observational cohort studies in the USA and Europe also suggest that the early starting of ART significantly lowers mortality related to HIV infection and AIDS.

BENEFIT TO THE PARTNER

HIV-transmission in couples is an important contributor to overall transmission rates, and the use of ART greatly reduces the risk of HIV-transmission to non-HIV-infected partners.

WORLD HEALTH ORGANIZATION

(WHO) has summarized the regimen in the "Programmatic Update – Use of Antiretroviral drugs for treating pregnant women and preventing HIV infection in infants" (April, 2012).[9] The 'Executive summary' of the guideline is as follows:

Now a new, third option (Option B+) after option A and option B, proposes further evolution—not only providing the same triple antiretroviral (ARV) drugs to all HIV-infected pregnant women beginning in the antenatal clinic setting, but also continuing this therapy for all of these women for life. While these benefits need to be evaluated in program settings, systems and support requirements need careful consideration, this is an appropriate time for countries to start assessing their situation and experience to make optimal programmatic choices.

OPTION 'B+' ADVANTAGES

Option B+ of lifelong ART for all HIV-infected pregnant women for the PMTCT has several advantages over option A or B, but needs to be evaluated in field and program settings:

- There is no need to stop ART after the birth of the baby or after the cessation of breastfeeding and risk of mother to child transmission has ceased
- Extended protection in future pregnancies for mother to child transmission from the very early stage
- Serodiscordant couples or partners will be benefitted by the intervention
- The client will be benefitted in two ways. First, regular stopping and starting in cases of high fertility with consequent development of more chances of drug resistance can be avoided. Secondly, the client will be benefitted by early start of treatment
- A simple and straight message to the community—that once ART is started—it should not be stopped.

CHALLENGES AND QUESTIONS

There are important programmatic, operational, and clinical challenges.

- ART service delivery in maternal and child health (MCH) and primary care settings
- Cost of the implementation
- Can it be sustainable in the long run?
- Adherence and retention in care in a comparatively healthier and younger clients
- Referral mechanisms and transition from the PMTCT program to HIV care and treatment program
- Concerns about the development of drug resistance with long-term use of ART initiated at a younger age
- Safety of increased ARV exposure for the fetus or infant
- Acceptability.

Considering the challenges, the programs or countries implementing option B+ should assess the feasibility and public health impact of the intervention.

Option B+ has important programmatic and operational advantages, which can help substantially decreasing the mother to child infection. And with the introduction of new guideline by WHO on use efavirenz among pregnant women and those of reproductive age; it will be much easier, safer, and beneficial in the long-term to implement option B+ in HIV+ pregnant mothers.

CONCLUSION

This is written on the experience of PMTCT (now EMTCT) about 2–5 years ago in a sub-Saharan country (with HIV prevalence of more than 20% in the general population and more than 40% in antenatal women) before any of the guidelines came out with option B+.

The main challenge was acceptance by the local population (particularly by the male partners), which was slowly overcome. Also the adherence issue, because the women had no health-related challenges before starting the therapy, which till date needs continuous counseling.

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