Antiretroviral therapy (ART) for treating HIV infection in ART-eligible pregnant women

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Three combination ART regimens (AZT/3TC/NVP; AZT/3TC/LPVr; and AZT/3TC/ABC) evaluated in the context of prevention of mother-to-child transmission of HIV in under resourced settings result in excellent early virological suppression in mothers and these regimens are relatively safe and well tolerated. All three regimens are available and listed in the national guidelines of most low- and middle-income countries and can be recommended for use in pregnant women who need ART.

RHL Commentary by Munderi P

1. INTRODUCTION

In many developing countries with generalized HIV epidemics, a significant proportion of HIV-positive adults who require antiretroviral therapy (ART) are women of childbearing age. At the same time, HIV infection in women is often diagnosed for the first time during a pregnancy, and an estimated 1.38 million pregnant women in low- and middle-income countries (90% of whom live in sub-Saharan Africa) are living with HIV and are in need of ART for the prevention of mother-to-child transmission (PMTCT) of HIV (1).

Antiretroviral therapy during pregnancy therefore has two complementary goals: to prevent the transmission of HIV to the unborn child; and to safeguard the health of the mother. This review (2) aimed to assess the best time to start ART during pregnancy and to evaluate the safest and most effective ART regimens for use during pregnancy.

2. METHODS OF THE REVIEW

The authors conducted a comprehensive search for analytical studies on the treatment of HIV infection during pregnancy, in which the subjects (pregnant women) were eligible for ART (as per WHO guidelines) and the ART regimens used were clearly described.

No studies were found that had specifically evaluated the optimal time to start ART during pregnancy, and none that described the long-term safety and effectiveness of ART in pregnant women.

The use of ART in pregnancy has however been evaluated in the context of studies in PMTCT and in this review, outcomes of MTCT studies are used as surrogate indicators of safety and efficacy of ART in pregnancy.
3. RESULTS OF THE REVIEW

Three randomized controlled studies (RCT) and six observational studies from the PMTCT context were selected for inclusion in the review. Only one of the RCTs selected had compared virological suppression in the mother with triple therapy ART regimens commenced during pregnancy. The Ma Baana Study was carried out in Botswana and included 730 HIV positive pregnant women with advanced HIV infection (CD4 counts below 200 cells/mm³). Of these, 560 were randomly assigned to receive either AZT/3TC/LPVr or AZT/3TC/ABC, while a control group of 170 women received AZT/3TC/NVP. In this study, ART was initiated early in the third trimester of pregnancy (24–36 weeks gestation) and HIV suppression in the mother determined at delivery and throughout the breast-feeding period (up to 6 months post partum). All three regimens resulted in excellent and comparable HIV virological suppression to below 400 copies per ml in the mothers at the time of delivery (96%, 93% and 94%, respectively) and throughout breast-feeding (92%, 93% and 95% respectively) (3).

The other studies had compared a triple therapy regimen with a prophylactic (short course) ART regimen to assess the risk of MTCT. They confirmed the higher efficacy of triple therapy ART in reducing MTCT, which may be taken as a surrogate indicator of superior HIV viral suppression. The Kesho Bora study, for example, included 824 women from Burkina Faso, Kenya and South Africa. Among 413 women who received AZT/3TC/LPVr the from 28th to 36th week of pregnancy until 6 months post partum, there was a 42% reduction in risk of HIV transmission to the women's infants, compared with women who received a short-course regimen of antenatal AZT/3TC alone supplemented by Nevirapine at the time of delivery (RR 0.58, 95%CI 0.34-0.97) (4). Similarly, in another RCT, the triple combination of AZT/3TC/NVP showed a superior reduction in risk of HIV transmission to the infant compared with the short course prophylactic regimen (5).

4. DISCUSSION

4.1 Applicability of the results

Three combination ART regimens evaluated in the context of PMTCT studies among pregnant women from resource limited settings result in excellent early virological suppression in the mother and are relatively safe and well tolerated. These regimens are AZT/3TC/NVP; AZT/3TC/LPVr and AZT/3TC/ABC. All three regimens are available and listed in the national guidelines of most low- and middle-income countries and can be recommended for use in pregnant women who need ART.

Even though none of the reviewed studies specifically evaluated the optimal time for starting ART during pregnancy, nor the long-term safety and effectiveness of ART in pregnancy, the goal of PMTCT is virological suppression in the mother; the therapeutic goal of ART in general is to achieve early HIV suppression and to sustain this suppression. The evidence garnered from the PMTCT context and presented in this review is therefore applicable also to the treatment of mothers for their own health in under-resourced settings.

The comparative safety during pregnancy of the two ARV drugs in the non-nucleoside reverse transcriptase inhibitor class of ARVs: EFV and NVP, is not addressed by this review nor by any of the studies that the authors summarized. This nevertheless remains an area of some uncertainty when considering treatment of women of childbearing age, because it is advised that EFV should not be used in early pregnancy since it carries some risk of toxicity to the fetus, while NVP has been associated with an increased risk of severe liver toxicity among women whose CD4 counts are above 250 cells/mm³. According to guidelines published by WHO, additional safety data are still being accumulated on these specific concerns (6).
4.2 Implementation of the intervention

An increasing number of women today, undergo HIV testing during the antenatal period and are offered antiretroviral drugs for PMTCT. An essential adjunct to this routine antenatal HIV testing should be assessment of the mother to ascertain eligibility for ART, with a view to commencing long-term combination ART for her own health. This assessment should consist of both a clinical assessment as an aid to staging HIV infection and CD4 count, where resources permit. Implementing this recommendation will require closer cooperation between maternal and child health services and HIV treatment programmes within national health systems. This would ensure continuity of HIV care and treatment for women across the prenatal and immediate and long-term postnatal periods.

With more widespread availability of ART in under-resourced settings, it is equally important to provide access to ART regimens that can safely be continued during pregnancy, in order to cater for incidental pregnancy occurring during the course of treatment. Stated desire for children increases significantly when the health outlook of HIV-positive women improves in the first 2?3 years of ART, as evidenced by a qualitative study among women of childbearing age in a Ugandan research cohort (7).

The widespread use of ART in under-resourced settings is a recent public health intervention. Consequently, it is essential to increase community awareness about the safety and benefits of ART for the health of the mother as well as for the prevention of MTCT through broader advocacy messages targeting women of childbearing age.

4.3 Implications for research

Since ART is a lifelong intervention, and as the review authors also suggest, more research is needed to define the long-term outcomes of ART, in particular the long-term safety of all antiretroviral drugs in pregnancy for women and their children.

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AZT: Zidovudine (INN) or azidothymidine
3TC: Lamivudine
NVP: Nevirapine
LPV/r: lopinavir/ritonavir
ABC: Abacavir
EFV: Efavirenz

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