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Is single-dose NVP relevant in the era of more efficacious PMTCT regimens? Lessons from Zambia

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For almost a decade, single-dose nevirapine (sdNVP) has been proven to be a safe and effective drug for the prevention of mother-to-child transmission (PMTCT) of HIV. With the advent of the use of more efficacious combination therapy strategy in reducing mother-to-child transmission, sdNVP has been relegated as a lower tier intervention. Availability of infrastructural capacity coupled with the practical reality that very few women attend an antenatal clinic more than once makes universal implementation of combination therapy a challenge. This retrospective review examined PMTCT programmatic indicators following the introduction of sdNVP at first contact in selected sites. Data from 79 PMTCT sites was reviewed from April 2006 to March 2007 (when sdNVP was offered only after 32 weeks) and compared to the period of April 2007–March 2008. In the pre-intervention period (April 2006–March 2007), the monthly average of pregnant women who received sdNVP per site was 5.02. Post-intervention (April 2007–March 2008), the monthly average increased by 59% to 7.97 (p-value <0.05). In pre-intervention period when sdNVP was dispensed at 32 weeks, the average proportion of pregnant women who received antiretroviral prophylaxis was 59%. This increased to 82% after the intervention. Current systems for dispensing sdNVP may be used as a foundation for implementation of more efficacious PMTCT regimens. The sdNVP administered at first contact should be a safety net for women who are unable to receive more efficacious regimen.

Keywords: HIV; perinatal; mother-to-child transmission; nevirapine; Zambia

Background and issue

For almost a decade, single-dose nevirapine (sdNVP) has been proven to be a safe and effective drug for the prevention of mother-to-child transmission (PMTCT) of HIV. The sdNVP regimen reduces transmission by over 40% (Ayouba et al., 2003; Guay et al., 1999; Jackson et al., 2003).

Concerns have been raised regarding the use of sdNVP on emerging resistant viral strains and consequently the effectiveness of NVP-containing highly active antiretroviral therapy (HAART) among HIV-infected women previously exposed to sdNVP. Decreased effectiveness has been demonstrated especially if HAART is initiated within six months of sdNVP exposure (Chi et al., 2007; Jourdain et al., 2004; Lockman et al., 2007). A meta-analysis conducted by Arrivé et al. (2007) reported the average estimate of NVP resistance prevalence for women using sdNVP (with or without other ante partum antiretrovirals (ARVs)) as 35.7%; for those women also provided postpartum ARVs, the average NVP resistance prevalence fell to 4.5%. To reduce NVP resistance, a short course of dual ARV regimen ZDV+3TC should be given to the mother postpartum (Arrivé et al., 2007).

With the advent more efficacious combination therapies to reduce MTCT, sdNVP has been relegated as a lower tier intervention, to be used if all else is not possible. While not the ideal, sdNVP does play an important role in preventing HIV transmission, particularly in the developing world. Availability of infrastructural capacity coupled with the reality that very few women attend an antenatal clinic more than once makes universal implementation of combination therapy a challenge.

In Zambia, for example, HIV prevalence is 14.3% and a significant proportion of HIV infections occur as a result of MTCT (Central Statistical Office [CSO], 2007). Since less than 50% of women in Zambia deliver their babies in health facilities (Ministry of Health [MOH], 2007), PMTCT combination therapy strategies provide a challenge. The sdNVP, used in tandem with more complex ARV prophylaxis regimens, allows for the greatest proportion of women to access to a form of ARV therapy for PMTCT.

In line with WHO guidelines, Zambia revised its National PMTCT protocol to recommend the use of Zidovudine (AZT) from 32 weeks and sdNVP

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at onset of labor as the minimum standard where HAART is not indicated or not feasible (MOH, 2006). However, in many remote areas of the country, the sdNVP regimen still forms the backbone of PMTCT programs. Current policy recommends that NVP tablets be distributed to HIV-positive women at 32 weeks of pregnancy – at the time of initiation of AZT (MOH, 2006). Many women, especially in peri-urban and rural areas, identified prior to the 32nd week of pregnancy do not return to the health facilities and are never dispensed a NVP tablet, leading to low uptake of ARV prophylaxis. In fact, program data from April 2006 to February 2007 revealed that approximately 40–50% of HIV-positive women do not return to a health center to receive sdNVP.

The Zambia Prevention Care and Treatment Partnership (ZPCT), a PEPFAR funded program, has been supporting implementation of PMTCT in rural areas of Zambia since 2005. ZPCT works in collaboration with Family Health International (FHI) and the Ministry of Health (MoH) to strengthen and expand existing HIV/AIDS services in five provinces: Northern, Luapula, Copperbelt, Central, and North-Western. At the end of March 2008, ZPCT was supporting PMTCT services in 199 facilities. To improve access to ARV prophylaxis for hard to reach women, in April 2007, ZPCT (in collaboration with the MoH and District Health Management teams) began dispensing sdNVP as soon as confirmation of HIV status was made, including to those clients before 32 weeks of gestation.

As part of PMTCT services, women tested HIV positive also receive counseling on how to reduce transmission to their infants, and are encouraged to return to antenatal clinic (ANC) for monitoring and to deliver in a health facility. Those who return for subsequent visits receive a more efficacious AZT-based prophylaxis regime – depending on their own health status. Pregnant women meeting criteria for full ART are put on HAART; those who do not yet have indication for HAART are given a short course ARV prophylaxis.

A review of the programmatic data was conducted to assess the administration of sdNVP at first contact within the context of implementation of a more efficacious regimen.

Methods

This review examined PMTCT programmatic indicators in ZPCT sites that were initiated before October 2007. Data from 79 PMTCT sites was reviewed from April 2006 to March 2007 (when sdNVP was offered only after 32 weeks), and compared to the period of April 2007–March 2008 (after the introduction of sdNVP at first contact).

PMTCT programmatic indicators using established routine Health Information Management Systems of the MoH are collected monthly from the Integrated Counseling and Testing/PMTCT Registers by Records Staff. It is then entered into an electronic database with inbuilt checks for accuracy. The submitted data is further reviewed for accuracy and completeness at the provincial level before submission to the central level. Routine quality data audits are performed at the site level to assure data quality.

Results

As expected, the average monthly number of women receiving sdNVP per site increased following the protocol change (Table 1). Since 40–50% of HIV-positive pregnant women never return for their 32-week appointment to collect and initiate AZT, sdNVP represented the only regimen they accessed. In the first time period, April 2006–March 2007, the monthly average of pregnant women who received sdNVP per site was 5.02. During the 12 months following the intervention, April 2007–March 2008, the monthly average jumped to 7.97 – a 59% increase (p-value <0.05) (Table 1).

Dispensing sdNVP at first contact allowed for a greater proportion of pregnant women in need of ARV prophylaxis for PMTCT to receive it (Figure 1). Between April 2006 and March 2007, during which sdNVP was dispensed at 32 weeks, the average proportion of pregnant women who received a complete course of ARV prophylaxis, including sdNVP, was 59% (out of those who tested positive and collected their results). Since dispensing at first contact, this average increased to 82% (from April 2007 to March 2008).

Discussion

In many developing countries in Eastern and Southern Africa such as Zambia, less than half of HIV-positive pregnant women access ARVs for PMTCT (Joint United Nations Programme on HIV/AIDS [UNAIDS], 2008). It is not uncommon for a woman to find out she is pregnant, test positive for HIV, and then not return to a health facility again until visiting an under five clinic with her infant. The median gestational age at the first ANC visit in Zambia is 22 weeks and almost a quarter of women do not return for the second or third visit when AZT should be initiated and, per the previous policy, sdNVP to be

Table 1. Average number of women who receive sdNVP per site.

	Period 1 (April 2006–March 2007)	Period 2 (April 2007–March 2008) post-protocol change	*p*-Value
Number of HIV+women receiving NVP	4763	7555	
Number of sites	79	79	
Mean number of women receiving NVP per site	5.02	7.97	<0.05
Uptake per month (NVP/HIV+) (%)	59	82	<0.05

dispensed (CSO, Central Board of Health, & ORC Macro, 2003).

The revised protocol to dispense sdNVP to women at first contact was an attempt to increase access to prophylactic ART for those women who would otherwise be lost. Without such a policy, approximately half of HIV-positive women would be without any ARV prophylaxis regimen to protect their babies. However, the success of this strategy depends on the continuous availability of trained staff. Staff attrition and turnover negatively affect its implementation.

Whether or not the women actually ingested the nevirapine tablets during labor is unknown. A study conducted in 2005 reported that 32% of HIV-infected women in Lusaka, Zambia, do not actually ingest the NVP tablet given to them during an ANC visit (Stringer et al., 2005). An increase in sdNVP dispensation does not necessarily translate into an increase in the number of women ingesting the NVP tablet.

The World Health Organization estimates that in circumstances where sdNVP is the only feasible option, its benefits outweigh the risks and should be administered (WHO, 2006). While not the most efficacious course of therapy for PMTCT, the sdNVP regimen enables access to ARV prophylaxis to pregnant women who would otherwise go without. The sdNVP is simple, easy to administer, and inexpensive.

PMTCT programs must consider the realities of the communities in which they serve. The sdNVP is an essential safety net for those women who do not return for regular ANC visits. Without the policy change to allow for dispensation at first contact, an unacceptably high proportion of pregnant women will not have access to ARV prophylaxis to prevent MTCT. The strategy ensures that any woman who attends ANC at least once will be afforded this basic intervention.

The fact remains that sdNVP remains the most feasible option in healthcare settings in many developing countries, particularly those which do not have capacity to measure hemoglobin at baseline and monitor patients on AZT for toxicity. Current systems for dispensing sdNVP may be used as a foundation for implementation of more efficacious PMTCT regimens. Countries should take advantage of their existing systems and strengthen them to provide more complex and efficacious regimens rather than starting from scratch.

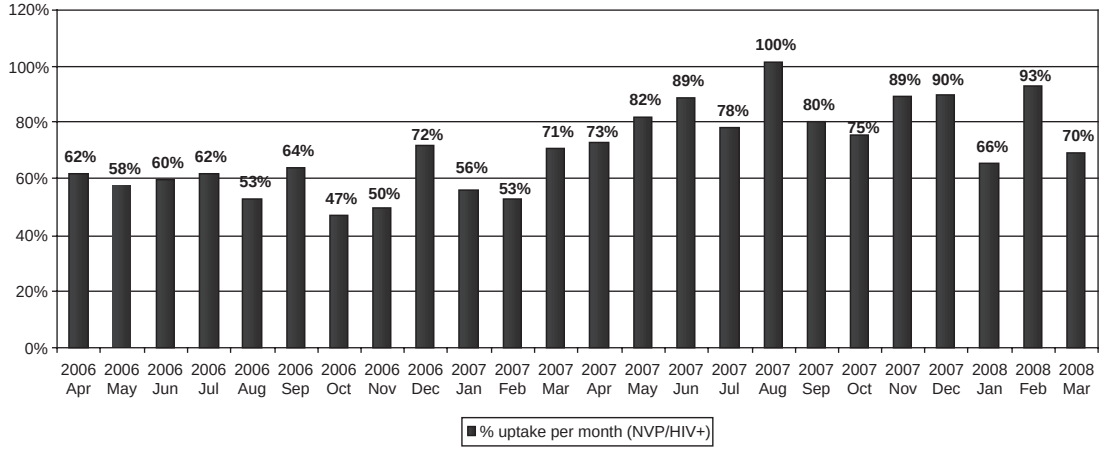

Figure 1. Proportion of pregnant women who received a complete course of ARV prophylaxis to reduce MTCT out of those who tested positive and collected their results [all months].

All effective strategies in the prevention arsenal need to be deployed to reduce pediatric HIV infection. While both infrastructural and human resource capacity must be developed to deliver more efficacious regimens, sdNVP should be available as a basic intervention and a strategy of last resort. While concerns over resistance in NVP-based ART are valid, they should not be used as an excuse for restricting sdNVP. Given the circumstances in many developing countries, by not offering sdNVP, a substantial number of women are essentially denied ARV prophylaxis. A somewhat less efficacious intervention is preferable to no intervention at all.

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