

### Effects of Depomedroxyprogesterone Acetate (DMPA) on systemic and lower genital tract HIV 1 viral loads in HIV positive ART naïve women attending a comprehensive care center in Kisumu Kenya

*Dr. Waithera Githendu, Principal Investigator • Human Pathology Resident  
University of Nairobi School of Medicine, Nairobi, Kenya.  
Supervised by Prof. Walter Jaoko, Prof. Christine Kigundu, Dr. Chris Gontier*



**Waithera Githendu**

*Dr. Githendu is a Human Pathology Resident at the University of Nairobi, College of Health Sciences. Her interests are microbiology (Virology) and HIV/AIDS research.*

*This research was supported with a grant from the International Society for Infectious Diseases (ISID).*

#### Background

Sub-Saharan Africa constitutes 65% of the global Human Immunodeficiency Virus and acquired immunodeficiency syndrome (HIV/AIDS) burden. Sixty percent of those infected are women, predominantly infected via heterosexual transmission. Contraceptives are very important in helping women make their reproductive health choices. The most commonly used of these are the hormonal contraceptives, which have been associated with increased risk of HIV transmission in women. The use of depomedroxyprogesterone (DMPA), in particular, has been associated with increased viral loads in plasma and lower genital tract, but this finding remains a contentious issue. Few studies have been done in this regard, analysing the effects of the contraceptive on plasma and lower genital tract HIV-1 viral loads. However, no human studies have been done to compare HIV-1 plasma and lower genital tract viral loads in DMPA users with viral loads of those not on DMPA. Furthermore, since HSV-2 is a known risk factor for HIV, information on the effect of HSV-2 seropositivity on plasma and lower genital tract in relation to DMPA use is needed.

#### Objectives

To determine the effects of DMPA on both plasma and lower genital tract HIV 1 viral loads in seropositive ART naïve women attending a comprehensive care centre (CCC) in Kisumu, Kenya, and to examine the impact of HSV-2 seropositivity on the viral load concentrations.

#### Design

Case control study.

#### Setting

This study used stored plasma and cervicovaginal lavage fluid samples obtained from participants in a previous study. These samples were obtained between August 2010 and January 2011 and were stored at an accredited laboratory in Kisumu, Kenya. The samples were then transported to the University of Nairobi laboratory for analysis.

#### Study Participants

Twenty one healthy cases of HIV-1 positive ART naïve women on DMPA and twenty one controls of healthy HIV-1 positive ART naïve women not on DMPA.

#### Analysis

Plasma and cervicovaginal lavage fluid HIV-1 viral loads were determined using automated real-time reverse transcriptase polymerase chain reaction and results reported as number of copies per millilitre.

#### Data Management

Viral loads were converted from number of copies/millilitre to  $\text{Log}_{10}$  for data analysis. Analysis was done using Stata v.12 for descriptive, univariate, bivariate and multivariate statistical analysis to examine for association between DMPA and plasma and lower genital tract viral loads, association between plasma and lower genital tract viral loads and duration of DMPA use and for association between the viral loads with HSV-2 seropositivity.

#### Results

The mean age of cases was 26 years and 28 years for controls. Cases had higher mean plasma viral loads (3.84) compared to controls (3.78) though this was not statistically significant. Cases also had higher lower genital tract viral loads compared to controls though the difference was not statistically significant. There was a statistically significant positive correlation between

*continued on next page*



## ISID Report of Waithera Githendu

Effects of  
Depomedroxyprogesterone  
Acetate (DMPA) on systemic  
and lower genital tract HIV 1  
viral loads in HIV positive  
ART naïve women attending  
a comprehensive care center  
in Kisumu Kenya

*This research was supported  
with a grant from the  
International Society for  
Infectious Diseases (ISID).*

## ISID Small Grant Report *continued*

plasma and lower genital tract viral loads in cases ( $r=0.464$ ) ( $p=0.002$ ) but no correlation in controls ( $r=0$ ). The median duration of DMPA use was 12 months. Duration of DMPA use had no statistically significant effect on plasma ( $p=0.520$ ) ( $p=0.562$ ) and lower genital tract viral loads ( $p=0.308$ ) ( $p=0.430$ ) on univariate and multivariate analysis respectively. 95.2% and 85.7% of the cases and controls were HSV-2 positive respectively. However, HSV-2 seropositivity had no statistically significant effect on plasma and lower genital tract viral loads, in both cases and controls even after adjusting for confounding factors.

### Discussion

The present study did not find a significant effect of DMPA on plasma viral loads even after adjusting for confounding factors. Although Cejtin et al had similar findings; their study looked at the effect of hormonal contraceptives in general and included both injectable and oral hormonal contraceptives unlike in the present study where only the effect of DMPA on plasma viral load was examined. However, the present finding contrasts with those by Lavreys et al, a prospective study, where newly HIV infected women on DMPA were found to have a higher viral set-point compared to the women not on DMPA.

This study found that there was an overall higher HIV viral load in the lower genital tract among the DMPA users than the non-DMPA users. Although not statistically significant, this could still be responsible for an increase in infectivity among these individuals therefore justifying use of dual contraception where barrier methods and DMPA are used concurrently. There is scarcity of data on the effects of DMPA on lower genital tract viral loads and most of the studies done in this regard have looked at effect of DMPA HIV-1 DNA shedding instead of HIV-1 RNA like in the present study. Although previous studies conducted in populations of African women have shown the use of hormonal contraceptives to be associated with increased pro-viral HIV-1 DNA cervical shedding, no association between hormonal contraception use and genital tract HIV-1 RNA shedding has been found. It can be speculated therefore that this pro-viral DNA in the cells is released into circulation and other compartments leading to high lower genital tract HIV-1 RNA viral shedding.

The present study correlated plasma and lower genital tract viral loads in DMPA users and plasma and lower genital tract viral loads in non-DMPA users. There was a positive correlation in DMPA users ( $r=0.464$ ,  $p=0.002$ ) but no correlation in non-DMPA users ( $r=0$ ). In cases, therefore, the higher plasma viral loads the higher lower genital tract viral loads. This finding is in agreement with several other studies in this regard. A study by Wagner et al demonstrated that a higher plasma viral load was associated with higher transudation of the virus into other compartments such as the lower genital tract.

The present study found no statistically significant correlation between duration of DMPA use and levels of plasma and lower genital tract viral loads. There was a time dependent increase in lower genital tract viral loads, although not significant. This may be attributed to the observation that women on DMPA have a time dependent reduction in the IL-1 $\beta$  and an increase in IL-10 levels in cervico-vaginal lavage leading to reduced proinflammatory response and polarisation to a less robust humoral immune activity, respectively. Contrasting studies have shown that DMPA used for shorter durations (4-6 months) leads to significantly higher viral loads at set point in both plasma and lower genital tract with tapering levels thereafter.

Despite the high prevalence of HSV-2 seropositivity among study subjects, the present study found no significant effect of HSV-2 on plasma and lower genital tract viral loads in both cases and controls even after adjusting for confounding factors. The lack of significant rise in viral loads could be attributed to the fact that most women, both cases and controls, were HSV-2 positive (cases 94%, controls 83%). This HSV-2 positivity could have led to higher lower genital tract cytokine concentrations leading to better local and systemic activation of the innate and humoral immunity against the HIV virus. Lavreys et al, however, found that the presence of genital urinary disease (GUD) during the early phase of HIV-1 infection was associated with a more rapid increase in plasma viral load during chronic HIV-1 disease.

### Recommendations

Larger more robust longitudinal studies are needed to clarify on the safety of DMPA in HIV positive women. In the meantime, use of dual contraception in HIV positive women is recommended.