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Original research article

Oral and injectable contraceptive use and HIV acquisition risk among women in four African countries: a secondary analysis of data from a microbicide trial☆,☆☆,★

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Abstract

Objective: To assess the effect of oral and injectable contraceptive use compared to nonhormonal contraceptive use on HIV acquisition among Southern African women enrolled in a microbicide trial.

Study design: This is a prospective cohort study using data from women enrolled in HIV Prevention Trials Network protocol 035. At each quarterly visit, participants were interviewed about self-reported contraceptive use and sexual behaviors and underwent HIV testing. Cox proportional hazards regression was used to assess the effect of injectable and oral hormonal contraceptive use on HIV acquisition.

Results: The analysis included 2830 participants, of whom 106 became HIV infected (4.07 per 100 person-years). At baseline, 1546 (51%) participants reported using injectable contraceptives and 595 (21%) reported using oral contraceptives. HIV incidence among injectable, oral and nonhormonal contraceptive method users was 4.72, 2.68 and 3.83 per 100 person-years, respectively. Injectable contraceptive use was associated with a nonstatistically significant increased risk of HIV acquisition [adjusted hazard ratio (aHR)=1.17; 95% confidence interval (CI) 0.70, 1.96], while oral contraceptive use was associated with a nonstatistically significant decreased risk of HIV acquisition (aHR=0.76; 95% CI 0.37,1.55).

Conclusion: In this secondary analysis of randomized trial data, a marginal, but nonstatistically significant, increase in HIV risk among women using injectable hormonal contraceptives was observed. No increased HIV risk was observed among women using oral contraceptives. Our findings support the World Health Organization's recommendation that women at high risk for acquiring HIV, including those using progestogen-only injectable contraception, should be strongly advised to always use condoms and other HIV prevention measures.

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Implications: Among Southern African women participating in an HIV prevention trial, women using injectable hormonal contraceptives had a modest increased risk of HIV acquisition; however, this association was not statistically significant. Continued research on the relationship between widely used hormonal contraceptive methods and HIV acquisition is essential.

Keywords: Hormonal contraception; HIV infection; Injectables; Oral contraceptive pills; Southern Africa; Women

1. Introduction

Access to safe and effective contraceptive methods is one of the cornerstones of reproductive health. Use of these methods has contributed to reductions in unintended pregnancies and improvements in maternal and child health outcomes throughout the world [1]. Approximately 140 million women use hormonal contraception (HC) globally, with 100 million using oral contraceptive pills (OCPs) and 40 million using injectable contraceptives [2]. After two decades of investigation, the relationship between injectable and oral HC and HIV acquisition remains unclear [3–8]. A prospective study of heterosexual HIV serodiscordant couples from seven African countries enrolled in an HIV prevention trial, which reported that women using injectable contraceptives had a 2.05-fold increased risk of HIV acquisition [95% confidence interval (CI) 1.04, 4.04], has refocused attention to this question [9]. Despite these findings and findings from several other studies that reported an increased risk of HIV acquisition among injectable HC users [10–15], the overall body of evidence assessing this relationship is still inconclusive [5–8], leading the World Health Organization (WHO) to call for further research on this topic [4]. Continued evaluation of the association between injectable and oral HC and HIV acquisition through well-designed secondary analyses using data from rigorously conducted, prospective HIV prevention studies has the potential to improve our understanding of this important public health issue [16]. Here we report the findings from a secondary analysis that assessed the effect of injectable and oral contraceptive use on HIV acquisition among women from four southern African countries enrolled in the HIV Prevention Trials Network (HPTN) 035 microbicide trial.

2. Methods

2.1. Study design, population and procedures

The HPTN 035 trial was a phase II/IIB, four-arm, multisite, randomized, controlled trial comparing BufferGel and 0.5% PRO 2000 gel against two comparator arms (hydroxycellulose placebo gel and no gel) for HIV prevention (#NCT00074425). Detailed trial methods have been described [17]. Briefly, between 2005 and 2008, women from five countries (Malawi, South Africa, USA, Zambia and Zimbabwe) were enrolled and followed for a minimum of 12 months and a maximum of 30 months, depending on enrollment date. Eligible women were at least 18 years of age, HIV-1 seronegative, nonpregnant and sexually active. All institutional review boards approved the trial at each site and all participants provided written informed consent.

Participants received a comprehensive HIV prevention package that included ongoing HIV risk reduction counseling, free male latex condoms and diagnosis and treatment of sexually transmitted infections (STIs) throughout the trial. Use of contraception was not required for study participation; however, participants at all research sites received contraceptive methods counseling. Participants in Malawi, Zambia and Zimbabwe were offered free contraceptive services at the research sites, while participants in South Africa were provided referrals to the nearest health center offering contraceptive services.

At monthly follow-up visits, a urine pregnancy test was performed. At quarterly visits, data were collected on self-reported condom use, sexual behaviors and contraceptive use (participants were asked "Which family planning method or methods are you currently using?"). Data on brand of injectable or oral contraceptives were not available. If a participant reported a change in method since her last visit, the self-reported date of change was systematically recorded on the medications log form. Blood was collected for HIV serologic testing at the quarterly visits. Herpes simplex virus type 2 (HSV-2) was evaluated at baseline and study exit visits.

2.2. Laboratory procedures

HIV-1 infection status was determined using a standardized algorithm, with initial testing conducted using rapid tests and confirmatory testing using western blot [17]. HSV-2 testing was performed using the HerpesSelect-2 EIA (Focus Technologies; Cypress, CA, USA). Vaginal saline microscopy was performed for the presence of motile trichomonads for diagnosis of *Trichomonas vaginalis*. Urine specimens were tested for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* annually using BD ProbeTec ET (Becton Dickinson; Franklin Lakes, NJ, USA).

2.3. Statistical analysis

Our primary aim was to estimate the association between self-reported injectable [depot medroxyprogesterone acetate (DMPA) or norethisterone enanthate (NET-EN)] or OCP use and HIV acquisition risk among African women enrolled in HPTN 035. The primary outcome was detection of HIV-1 infection. Participants who reported using contraceptive implants were excluded from the analysis due to small numbers. In addition, we excluded women enrolled at the US site as there were no