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Willingness of Kenyan HIV-1 serodiscordant couples to use antiretroviral based HIV-1 prevention strategies

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Abstract

Introduction—Antiretroviral treatment (ART) and pre-exposure prophylaxis (PrEP) have demonstrated efficacy as new HIV-1 prevention approaches for HIV-1 serodiscordant couples.

Methods—Among Kenyan HIV-1 serodiscordant heterosexual couples participating in a clinical trial of PrEP, we conducted a cross-sectional study and used descriptive statistical methods to explore couples' willingness to use antiretrovirals for HIV-1 prevention. The study was conducted prior to July 2011, when studies among heterosexual populations reported that ART and PrEP reduced HIV-1 risk.

Results—For 181 couples in which the HIV-1 infected partner had a CD4 count ≥350 cells/μL and had not yet initiated ART (and thus did not qualify for ART under Kenyan guidelines), 60.2% of HIV-1 infected partners (69.4% of men and 57.9% of women) were willing to use early ART (at CD4 ≥350 cells/μL) for HIV-1 prevention. Among HIV-1 uninfected partners, 92.7% (93.8% of men and 86.1% of women) reported willingness to use PrEP. When given a hypothetical choice of early ART or PrEP for HIV-1 prevention, 52.5% of HIV-1 infected participants would prefer to initiate ART early and 56.9% of HIV-1 uninfected participants would prefer to use PrEP.

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Conclusions—Nearly 40% of Kenyan HIV-1 infected individuals in known HIV-1 serodiscordant partnerships reported reservations about early ART initiation for HIV-1 prevention. PrEP interest in this PrEP-experienced population was high. Strategies to achieve high uptake and sustained adherence to ART and PrEP for HIV-1 prevention in HIV-1 serodiscordant couples will require responding to couples' preferences for prevention strategies.

Keywords

HIV prevention; antiretrovirals; pre-exposure prophylaxis; Africa; couples

Introduction

Antiretroviral-based HIV-1 prevention strategies – specifically, antiretroviral treatment (ART) to reduce the infectiousness of HIV-1 infected persons (including when initiated at CD4 counts at or above current WHO guidelines) and pre-exposure prophylaxis (PrEP) to protect HIV-1 uninfected persons from HIV-1 acquisition – are among the most promising new approaches for decreasing HIV-1 spread.[1] Stable HIV-1 serodiscordant couples are central to the African HIV-1 epidemic and could be a prime target population for antiretroviral-based HIV-1 prevention; results of landmark clinical trials have recently demonstrated substantial efficacy for these strategies to reduce HIV-1 risk in this population.[2,3] To limit costs, policies for ART and PrEP in couples could recommend staged use – e.g., PrEP until the HIV-1 infected partner initiates ART – rather than concurrent use of both strategies in the same couple.[4] Thus, understanding couples' preferences for and concerns about antiretrovirals for HIV-1 prevention is important to inform guidelines for the use of early ART and PrEP.

Methods

We conducted a cross-sectional study among a convenience sample of HIV-1 heterosexual serodiscordant couples to determine preferences for and willingness to use antiretrovirals for HIV-1 prevention. Eligible couples were participants from the Thika, Kenya site in the Partners PrEP Study, a randomized clinical trial of daily oral tenofovir (TDF) and combination emtricitabine (FTC)/TDF PrEP to prevent HIV-1 acquisition by HIV-1 uninfected members of heterosexual HIV-1 serodiscordant couples. Study procedures have been described elsewhere.[5] At an interim review in July 2011, the Partners PrEP Study independent Data and Safety Monitoring Board recommended that the placebo arm of the trial be discontinued early due to clear demonstration of PrEP efficacy for HIV-1 prevention.[3]

Data for this cross-sectional study were collected between March and July 2011, prior to the announcement of PrEP efficacy in heterosexual populations.[6,7] During this time, the HPTN 052 trial demonstrated that early ART (initiated at CD4 counts of 350–550 cells/μL) reduced HIV-1 risk by 96% in HIV-1 serodiscordant couples and the FEM-PrEP study closed early due to an inability to demonstrate efficacy for FTC/TDF to prevent HIV-1 acquisition.[2,8] Participants were informed and counseled about results from each of these studies. For the present study, participants were individually invited by study staff during a routine quarterly clinical trial visit to answer questions about HIV-1 prevention; some participants attended the study visit with their study partner while others attended separately due to conflicting work constraints or partnership dissolution. Couples were eligible if the HIV-1 uninfected partner had not seroconverted to HIV-1 prior to the study visit (i.e., the couple was still HIV-1 serodiscordant). Written informed consent for this study was obtained and interviews were conducted with each member of the couple separately. The

study protocol was approved by the University of Washington and Kenyatta National Hospital institutional review boards.

The primary analysis group was couples for which both members completed the interviewer-administered questionnaire (to enable analysis of agreement within couples), both indicated that they were still a couple, and the HIV-1 infected partner had a CD4 count ≥350 cells/μL (and was therefore ineligible for ART under current Kenyan policies and WHO guidelines) and had not initiated ART. Thus, this primary analysis group could potentially be a target for early ART and/or PrEP for HIV-1 prevention. Analyses were also conducted for all participants who completed the questionnaire.

To assess participant's long term willingness to use PrEP, HIV-1 uninfected participants were asked “if we find that PrEP works to keep people free from HIV, would you be willing to take PrEP tablets every day for the next five years.” To assess willingness to initiate ART for HIV-1 prevention purposes, HIV-1 infected partners were asked “would you be willing to start antiretrovirals before your CD4 count reaches 350 if it would lower your chance of giving HIV to your partner?” In open-ended questions, participants were asked to describe their top concerns about early ART or PrEP. All participants were also asked to declare a preference for early ART or PrEP.

We used descriptive methods to analyze couple's preferences and willingness to use antiretroviral-based HIV-1 prevention and logistic regression to determine if any demographic, behavioral or clinical characteristics were associated with willingness to initiate antiretroviral-based HIV-1 prevention. Data were analyzed using SAS version 9.2.

Results

Participant characteristics

367 HIV-1 infected and 405 HIV-1 uninfected participants completed the questionnaire (Table 1). Couples completing the questionnaire had been partners for a median of 5.6 years (IQR 2.1–11.0) and enrolled in the Partners PrEP Study for about 21 months (IQR 15–27). Less than 20% of all participants no longer considered themselves a couple with their study partner and 20.6% of HIV-1 infected participants had already initiated ART due to clinical or immunologic (CD4) indicators. In total, 181 couples were included in our primary analysis group because both partners completed the questionnaire and indicated their continuing partnership and the HIV-1 infected partner had a CD4 count ≥350 cells/μL and had not yet initiated ART.

Willingness and preferences for antiretroviral-based HIV-1 prevention

Among 181 couples in the primary analysis group, 69.4% and 57.9% of HIV-1 infected men and women indicated willingness to initiate ART before their CD4 count reached 350 cells/μL and 93.8% and 86.1% of HIV-1 uninfected men and women would be willing to use PrEP (Table 2). Willingness was similarly high among all participants who completed the questionnaire. Willingness to use antiretrovirals for HIV-1 prevention before versus after May 2011 (when results from the HPTN 052 trial were publically announced) was similar in the primary analysis group (p=0.7, Cochran-Armitage trend test).

In the primary analysis population, 61.1% of HIV-1 infected male participants indicated a preference for themselves to initiate ART early. HIV-1 infected women in this population were split between preferring to initiate early ART themselves (50.3%) and having their partner use PrEP (49.7%). HIV-1 uninfected participants slightly preferred PrEP use for themselves over ART use for prevention by their HIV-1 infected partner (57.2% of men and 55.6% of women). In 26.0% of couples, both members preferred to have the HIV-1

uninfected partner use PrEP and in 21.5% of couples, both members preferred to have the HIV-1 infected partner initiate ART.

Participant concerns about antiretroviral-based HIV-1 prevention

Among HIV-1 infected participants in our primary analysis population who were unwilling to initiate early ART for HIV-1 prevention (n=72), the primary concerns were side effects (a concern of 51.4% of those unwilling), stigma (20.8%), pill burden (19.4%) and the potential for earlier development of antiretroviral resistance (18.1%). Men and women had similar concerns. Among HIV-1 uninfected participants, 14 (7.7%) were unwilling to use PrEP and their primary concerns were that 5 years would be too long (6/14 of those unwilling), people should not take drugs unless they are sick (3/14 of those unwilling), side effects (3/14 of those unwilling), and drug fatigue (2/14 of those unwilling). Logistic regression did not identify any characteristics that were significantly associated with willingness to use early ART or PrEP, including gender, sexual behavior, fertility desires, contraceptive use, risk perception of acquiring/transmitting HIV-1, and, for HIV-1 infected partners, CD4 count and WHO stage (data not shown).

Discussion

In this cohort of Kenyan HIV-1 serodiscordant couples that received regular counseling about HIV-1 prevention, including counseling about the importance of ART for treatment and prevention, 40% of ART-naïve and ineligible HIV-1 infected individuals were unwilling to consider initiating ART early for HIV-1 prevention purposes. Similar to prior work on ART acceptability in Africa, side effects were a top concern for participants.[9–11] This population was experienced with and well-informed about PrEP and 90% of HIV-1 uninfected participants said they would be willing to use PrEP on a long-term basis. When given a hypothetical choice of ART or PrEP for HIV-1 prevention, participants tended to choose the prevention option that they would control themselves (HIV-1 uninfected participants chose PrEP and HIV-1 infected participants chose ART).

Numerous studies from diverse settings have identified structural and social challenges leading to lower than expected rates of ART initiation among adults meeting eligibility criteria. While structural challenges, such as accessing HIV-1 testing, enrolling in HIV-1 care programs, and receiving CD4 test results,[12] are being addressed through programs to strengthen health systems, concerns about side effects, stigma, and perceptions that ART is only for sick people may prevent individuals' from accessing ART and need to be addressed through counseling and community sensitization.[13] Early ART implementation, even among HIV-1 serodiscordant couples who recognize their own HIV-1 risk, will need to address the perceptions couples have of ART use, including its risks and benefits. Our data from the entire population of couples, including ART-experienced couples, indicate a higher level of ART willingness by the HIV-1 infected partner, which likely reflects more comfort with ART for those with lower CD4 counts, symptomatic disease, and, most importantly, personal experience with ART use.

A possible HIV-1 prevention strategy for serodiscordant couples that will utilize both ART and PrEP is for the HIV-1 uninfected partner to use PrEP until the HIV-1 infected partner is willing and able to initiate ART.[4] Such a strategy may be cost-effective, provide HIV-1 infected partners an opportunity to decide when to start ART, and may allow a “bridge period” for a few months after the infected partner starts ART, when transmission risk may still be high because viral load is not yet suppressed. Our study was conducted prior to the widespread announcements about the high efficacies of ART and PrEP for prevention, demonstrated in clinical trials of HIV-1 serodiscordant couples.[2,3] Couples' preferences may evolve over time as prevention and treatment guidelines are developed and

implemented.[14,15] Continued assessment of couples' preferences and actual use of antiretroviral-based HIV-1 prevention strategies will be important to ensure an optimal prevention impact.

Our study was conducted among HIV-1 serodiscordant couples who were very aware of the potential benefits of antiretrovirals for HIV-1 prevention, especially PrEP, and thus our results likely reflect a greater level of willingness to use PrEP than would be found in a non-clinical trial population. Similar studies should be conducted among couples who are just learning their HIV-1 serodiscordant status and are less familiar with HIV-1 prevention strategies. Future studies of this question will also benefit from following couples to identify trends in willingness, uptake of antiretrovirals, and the inclusion of qualitative methods to gain a deeper understanding of individuals' and dyadic preferences of these novel prevention methods. In addition, studies among HIV-1 infected and uninfected individuals lacking knowledge of their partner's HIV-1 status should be conducted.

Successful implementation of antiretroviral-based HIV-1 prevention for HIV-1 serodiscordant couples will need to be targeted to couples at highest risk for transmission who are also willing to initiate and adhere to daily antiretrovirals. In our study, not all couples would be willing to use ART prior to the HIV-1 infected partner having clinical symptoms and a perceived need for initiation; PrEP could be a suitable alternative for these couples. As antiretroviral-based HIV-1 prevention strategies are incorporated into prevention policies and programs, it will be important to understand and accommodate couples' preferences and willingness to use antiretroviral-based HIV-1 prevention.

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Table 1

Participant characteristics*

	Couples with HIV-1 uninfected men		Couples with HIV-1 uninfected women	
	HIV-1 uninfected men	**HIV-1 infected women**	**HIV-1 uninfected women**	**HIV-1 infected men**
Eligible to participate	379	377	112	111
Enrolled prior to July 2011 (N, % of eligible)**	285 (75.2%)	312 (82.8%)	82 (73.2%)	93 (83.8%)
Months since enrollment in Partners PrEP Study (median, IQR)	21 (15 – 27)	21 (15 – 27)	21 (12 – 24)	21 (15 – 27)
Still a couple with study partner (N, %)	243 (85.3%)	253 (82.1%)	67 (81.7%)	72 (80.0%)
Age, years (median, IQR)	34.5 (29.8 – 40.8) :	29.5 (25.1 – 34.4)	33.0 (27.1 – 39.8)	38.2 (34.2 – 44.6)
Children with study partner (median, IQR)	2 (0 – 3)		2 (0 – 3)	
Partnership duration, years (median, IQR)	4.4 (1.8 – 9.9)		10.0 (4.2 – 19.7)	
On ART at the time of data collection (N, %)	59 (18.9)		24 (25.8)	
Not on ART and not eligible for ART*** (N, %)	203 (65.1)		54 (58.1)	

* Couples were offered enrollment separately – 323 couples (250 with HIV-1 uninfected men and 73 with HIV-1 uninfected women) had participation from both members.

** Data analysis included only couples who enrolled prior to the placebo arm discontinuation of the Partners PrEP Study in July 2011.

*** Under current Kenyan ART guidelines.

Table 2

Willingness and preferences for ART-based HIV-1 prevention

	Couples with HIV-1 uninfected men		Couples with HIV-1 uninfected women	
	HIV-1 uninfected men	**HIV-1 infected women**	**HIV-1 uninfected women**	**HIV-1 infected men**
Primary analysis group *				
Number of participants	145	145	36	36
Willing to use early ART		84 (57.9)		25 (69.4)
Willing to use PrEP	136 (93.8)		31 (86.1)	
Prefers early ART initiation	62 (42.8)	73 (50.3)	16 (44.4)	22 (61.1)
Prefers PrEP	83 (57.2)	72 (49.7)	20 (55.6)	14 (38.9)
All enrolled				
Number of participants	285	312	82	93
Willing to use early ART		205 (66.6)		67 (75.3)
Willing to use PrEP	257 (90.2)		68 (82.9)	
Prefers early ART initiation	128 (44.9)	190 (61.7)	38 (46.3)	65 (73.0)
Prefers PrEP	157 (55.1)	118 (38.3)	44 (53.7)	24 (27.0)

* The primary analysis group was defined as participants for which both members of the couple completed the questionnaire, both considered themselves still in a partnership with each other, and the HIV-1 infected partner had a CD4 count >350 cells/μL and had not yet initiated ART.