

Use of postexposure prophylaxis against HIV infection following sexual exposure does not lead to increases in high-risk behavior

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Background: The effectiveness of postexposure prophylaxis (PEP) following occupational exposure to HIV has prompted advocacy for PEP following sexual or drug-use exposures.

Objective: To evaluate the concern that the availability of PEP for sexual or drug-use exposures might result in behavioral disinhibition.

Design: Non-randomized trial of 397 adults with high-risk sexual or drug-use exposures within the prior 72 h.

Interventions: Antiretroviral medication for 4 weeks and five counseling sessions.

Main outcome measurements: Participants were followed for 12 months for repeat request for PEP and for changes compared with pre-enrollment in overall high-risk behavior and the acquisition of sexually transmitted diseases (STD) and HIV.

Results: After 12 months following receipt of PEP, the majority of participants (83%) did not request a repeat course of PEP. At 12 months after exposure, 73% of participants reported a decrease compared with baseline in the number of times they had performed high-risk sexual acts; 13% reported no change, and 14% had an increase. Most participants (85%) had no change in the incidence of STD; 8.5% had a decrease and 6.8% an increase. Three homosexual men seroconverted for HIV (none associated with the presenting exposure) for a rate of 1.2/100 person-year, equivalent to rates in San Francisco among all homosexual men.

Conclusions: After receipt of PEP consisting of antiretroviral medication and behavioral counseling following a potential sexual exposure to HIV, most individuals do not increase high-risk behavior. Coupled with prior safety and feasibility data, this lack of behavioral disinhibition suggests that use of PEP should be routinely considered following high-risk sexual exposures.

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Introduction

Postexposure prophylaxis (PEP) with antiretroviral medications is recommended by the US Public Health Service following occupational exposure to HIV [1]. The effectiveness of PEP in the occupational setting [2], coupled with efficacy data following genital tract exposures in animal models [3], has prompted advocacy for the use of PEP following non-occupational exposures in humans via sexual contact or injection drug use. Although there are sufficient similarities between occupational and non-occupational exposures to consider extrapolating the biological efficacy of PEP in the occupational setting to non-occupational exposures (e.g., roughly equivalent infectivity per exposure [4]), there are critical contextual differences that must be addressed before PEP for non-occupational exposures can be routinely recommended. One important difference is the concern that the availability of PEP following sexual or drug-use exposure could promote increases in high-risk behavior, with repeated requests for PEP. Although PEP for non-occupational exposures is now being used both in the United States [5–9] and abroad [10–21], there are no data evaluating potential resultant behavioral disinhibition. To address this, this 1-year study followed individuals who had received PEP following a sexual or injection drug-use exposure and evaluated demand for repeat use of PEP, overall changes in high-risk behavior, and the acquisition of HIV infection and other sexually transmitted diseases (STD).

Methods

Overall design and participants

A full description of the design has been previously reported [8]. In brief, HIV-negative individuals reporting a potential exposure to HIV in the prior 72 h, outside of the occupational setting, were enrolled in a feasibility study of PEP. All participants were offered 28 days of combination antiretroviral therapy; only those who elected to initiate medications were included in this analysis. All participants also received five sessions of risk-reduction counseling (at study entry and at 1, 2, 4, and 5 weeks after exposure). These sessions were individually tailored based on social cognitive theory, incorporating strategies from motivational interviewing and coping effectiveness training [22–24]. All participants were subsequently evaluated at 6 and 12 months following exposure. Up to four repeat administrations of PEP for subsequent exposures were provided within the 12 months following initial exposure.

The protocol used in this study was approved by the

University of California, San Francisco, Committee on Human Research.

Measurements

Participants were assessed by a structured interview, at study entry and at 6 and 12 months following entry, regarding their sexual behavior and recreational drug use in the previous 3 months, and for aspects of their mental health. Depression was measured using a modified version of the Center for Epidemiologic Studies Depression Scale [25,26] and stress was evaluated using the Perceived Stress Scale [27]. For these scales, the distribution of responses was broken into quartiles, with the highest quartile consisting of individuals with scores most associated with depression and stress, respectively.

Individuals who resided in San Francisco County, regardless of whether they returned for study visits, were cross-referenced to the database of STD maintained by the San Francisco Department of Public Health. HIV seroconversion was determined for all participants with standard techniques at 6 and 12 months postexposure.

Statistical analysis

Kaplan–Meier methods were used to estimate the probability of participants undergoing a subsequent exposure and repeat use of PEP during the year following the initial receipt of PEP. Proportional hazards regression was used to estimate the relative risk of repeat use of PEP associated with various participant characteristics. In determining changes in sexual behavior following receipt of PEP, the number of times a particular act was practiced prior to a follow-up visit (either at 6 or at 12 months) was compared with that reported at baseline for each participant. The sign test was used to evaluate statistically whether the number of participants found to have a decrease in the practice of a particular act was different from the number found to have an increase. In these analyses, a high-risk partner was anyone whom the participant reported as HIV infected or for whom the participant was uncertain about HIV infection status. A high-risk act was defined as unprotected insertive or receptive anal or vaginal intercourse, or oral intercourse with receipt of ejaculate.

Results

Of 401 participants who presented with eligible exposures, all but four elected to use antiretroviral medication. The characteristics of the 397 who were prescribed medication were similar to those reported for the entire group [8]. In brief, the median age was 32 years and the majority (91%) were men. Of the

men, 334 (92%) reported to be men who have sex with men (MSM) and 29 were heterosexual. The majority (372; 94%) reported a sexual exposure and three (0.76%) reported a dual sexual and injection drug exposure. Only eight individuals (2.0%) reported an isolated drug-use exposure. Nine individuals (2.3%) reported a needle stick not involving self-administration of drugs (usually at a needle exchange site) and five individuals (1.3%) reported exposure through non-sexual assault. At 6 months postexposure, 298 (75%) participants were available for evaluation, and at 12 months, 266 (67%) were available.

Repeat administration of prophylaxis

Within 1 year following their initial receipt of PEP, 55 participants [17% by Kaplan–Meier estimation; 95% confidence interval (CI), 13–21] had at least one exposure accompanied by repeat administration of PEP; this was an average rate of 5.1% (95% CI, 3.8–6.6) of participants per 3-month period. Nine participants received two repeat courses of PEP; five participants received three repeat courses, and one participant received four repeat courses. Of the 77 repeat courses of PEP, 72 (94%) were for sexual exposures, two (2.6%) were for dual sexual and injection drug exposures and three (3.9%) were for needle sticks not involving self-administration of drugs. The majority (90%) of repeat PEP administrations were provided by the study with the remainder obtained from friends or a personal physician.

As context to interpret the observed frequency of repeat PEP use, it was determined that 162 of 395 evaluable participants (41%; 95% CI, 36–46) reported engaging in at least one act (in addition to the act that prompted entry into the study) that would have met eligibility criteria to receive PEP in the 3 months prior to enrollment. Therefore, the observed frequency of engaging in a high-risk act with repeat use of PEP in the period following initial receipt of PEP was significantly lower than the frequency of high-risk activity that might have normally occurred in this population.

When examining baseline participant characteristics associated with repeat use of PEP, depression, greater number of prior high-risk sexual partners, and lower education were independently associated with repeat administration of PEP (data not shown).

Change in sexual behavior at 6 and 12 months

In the year following receipt of PEP, there was a marked reduction in the overall practice of high-risk acts with high-risk partners (Fig. 1). At 6 months following receipt of PEP, 77% of MSM reported a decrease compared with baseline in the number of times they had performed any high-risk act with a high-risk partner, 15% reported no change and only 8% reported an increase ($P < 0.001$, comparing the

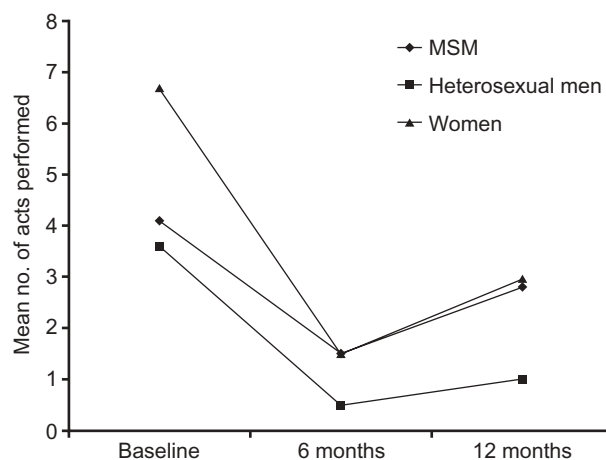


Fig. 1. Effect of postexposure prophylaxis (PEP) on high-risk sexual acts. Mean number of times participants engaged in either unprotected receptive or insertive anal or vaginal intercourse, or oral intercourse with receipt of ejaculate with high-risk partners in the 3-month period prior to receipt of PEP (baseline) and in the 3-month period prior to the 6- and 12-month visits following receipt of PEP.

number reporting a decrease with those reporting an increase). At 12 months, 76% reported a decrease, 11% no change, and 13% an increase ($P < 0.001$). Examination of specific sexual acts showed similar findings (Table 1).

Development of a sexually transmitted disease

Of the 293 participants residing in San Francisco, 27 (9.2%) had a STD recorded in the San Francisco Department of Public Health STD registry in the year prior to enrollment, and 21 (7.1%) had a recorded STD in the year subsequent to receipt of PEP. Overall, comparing the total number of STD recorded in the year following study entry with that of the year before entry, 85% of participants had no change, 8.5% had a decrease, and 6.8% had an increase. This overall pattern was also observed when MSM, heterosexual men, and women were examined separately.

HIV seroconversion

Four participants (three MSM and one woman) seroconverted for HIV antibodies over the year. For MSM, HIV seroincidence was 1.2/100 person-years (95% CI, 0.3–3.1). For reference, the incidence estimated among all MSM in San Francisco was 1.04/100 person-years in 1997 and 2.2/100 person-years in 2000 [28]. Incidence estimates for heterosexual men (0/100 person-years; 95% CI, 0–17.1) and women (4.0/100 person-years; 95% CI, 0.2–18.0) were less precise. All participants who developed HIV infection were seronegative at their 6-month visit and seropositive at 12 months, suggesting that infection was neither the

Table 1. Change in participants' reported number of high-risk sexual acts with high-risk partners at 6 and 12 months following receipt of postexposure prophylaxis compared with that for the baseline period prior to prophylaxis.

Group and intercourse act	Comparison of 6 months with baseline				Comparison of 12 months with baseline			
	Decrease [No. (%)]	No change [No. (%)]	Increase [No. (%)]	<i>P</i> value ^a	Decrease [No. (%)]	No change [No. (%)]	Increase [No. (%)]	<i>P</i> value ^a
Men who have sex with men								
Receptive anal	127 (51)	105 (42)	16 (6.5)	< 0.001	111 (51)	92 (42)	14 (7.3)	< 0.001
Insertive anal	112 (46)	109 (45)	21 (8.7)	< 0.001	103 (48)	83 (39)	29 (13)	< 0.001
Receptive oral ^b	45 (19)	181 (75)	15 (6.2)	< 0.001	43 (20)	156 (74)	12 (5.7)	< 0.001
Heterosexual men								
Insertive vaginal	11 (52)	9 (43)	1 (4.7)	0.006	9 (50)	6 (33)	3 (17)	0.15
Insertive anal	0 (0)	19 (100)	0 (0)	> 0.99	0 (0)	17 (100)	0 (0)	> 0.99
Women								
Receptive vaginal	16 (67)	6 (25)	2 (8.3)	0.001	15 (65)	5 (22)	3 (13)	0.008
Receptive anal	2 (9)	19 (86)	1 (4.5)	> 0.99	3 (14)	18 (86)	0 (0)	0.25
Receptive oral ^b	3 (14)	18 (86)	0 (0)	0.25	3 (14)	18 (86)	0 (0)	0.25

^a*P* value is for the sign test, which compares the number of participants reporting a decrease (versus baseline) in the number of acts performed at the follow-up visit to the number of participants reporting an increase in the number of acts. ^bReceptive oral intercourse is limited to acts involving participants' receipt of partner's ejaculate.

result of the initial exposure nor of chemoprophylactic failure.

Discussion

For PEP to be a useful intervention for the prevention of HIV infection following sexual or drug-use exposures, it needs to be feasible, safe, and efficacious. Our prior work has shown that providing PEP, consisting of both antiretroviral medication and behavioral counseling, for non-occupational exposures is feasible; although subjective toxicity is frequent, biochemical toxicity is rare with the regimens we prescribe [8]. The evaluation of safety, however, must extend beyond the period where medications are used. Indeed, the most substantial concern about PEP for non-occupational exposures is whether its availability will encourage high-risk behavior and repeated demand for PEP. The present study dispels this concern and demonstrates that most individuals do not experience sexual behavior disinhibition after receipt of PEP that includes both antiretroviral medication and risk-reduction counseling.

Examining individuals who have received PEP following a sexual exposure, and, therefore, by definition are knowledgeable about its availability, presents a good opportunity to evaluate PEP-related behavioral disinhibition. We focused on repeat exposures accompanied by a repeat request for PEP as potentially being caused by PEP-related behavioral disinhibition because we believe it is unlikely that knowledge of PEP availability would result in increased practice of high-risk acts that are unaccompanied by a request for PEP. In other words, the only high-risk exposures that can be reasonably suspected to be attributable to PEP availability are

those exposures for which individuals request PEP. The majority (83%) of participants did not undergo a repeat exposure accompanied by request for PEP. Even among the 17% who did, it is uncertain whether PEP availability, rather than continuation of usual behavior, motivated the act. Indeed, the facts that most of the participants who underwent repeat PEP use had a history of high-risk behavior prior to enrollment and that prior high-risk behavior was the strongest risk factor for repeat use of PEP suggest that individuals who requested repeat courses of PEP may have been simply exhibiting their usual pattern of high-risk behavior.

Because of concerns that the availability of PEP could result in behavioral disinhibition and because we believe that request for PEP represents an effective moment in terms of education for future risk reduction, we provided risk-reduction counseling in addition to antiretroviral medications. The counseling, however, was resource intensive, and whether our results would be observed without such counseling is unknown.

Direct proof of the efficacy of non-occupational PEP in preventing HIV transmission is still needed. Although we saw no instances of chemoprophylactic failure, we would not have necessarily expected to observe any HIV seroconversions associated with the presenting exposures even without the provision of PEP, given our sample size, the low per-exposure infectivity of HIV and the likelihood that some participants had contact with uninfected sources. Therefore, our data should not be taken as evidence for the efficacy of PEP in preventing seroconversion. Unfortunately, definitive ascertainment of the efficacy of PEP following a sexual exposure through randomized placebo-controlled trials will be difficult because

of the large sample size required. Until direct evidence regarding efficacy is available, decisions must nonetheless be made on how to manage individuals with high-risk sexual exposures. Given the indirect evidence of efficacy gleaned from the occupational setting and from animal studies, coupled with our findings on feasibility and safety, we believe that PEP, comprising both antiretroviral medication and risk-reduction counseling, should be routinely considered following high-risk sexual exposures.

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