

HIV postexposure prophylaxis-in-pocket: long-term follow-up of individuals with low-frequency, high-risk HIV exposures

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See related paper on page 481

Background: HIV preexposure prophylaxis and postexposure prophylaxis are two major biomedical HIV prevention modalities. The utility of these prevention tools for individuals with infrequent high-risk HIV exposures remains uncertain. HIV post-exposure prophylaxis-in-pocket ('PIP') may be an effective HIV prevention tool in such situations. Here, we present long-term follow-up of a cohort of patients initiated on PIP for HIV prevention.

Methods: We retrospectively evaluated clinical characteristics of patients initiated on PIP as a primary HIV prevention tool between 1 January 2016 to 31 May 2019 at the Toronto General Hospital HIV Prevention Clinic and St. Michael's Hospital HIV Clinic, both in Toronto, Canada. Patients were referred for consideration of a biomedical HIV prevention modality. Individuals with a low frequency of high-risk exposures to HIV were initiated on PIP after counselling, and were followed at regular intervals. Demographic and clinical data was collected with a standardized form.

Results: In total, 79 patients were initiated on PIP as a primary HIV prevention modality and followed for a mean duration of 14.8 months combining for a total of 97.3 patient-years. Twenty-one (26.6%) patients used their PIP, and 32 courses of PIP were taken during the study period. Transitions between HIV prevention modalities included 13 (16.5%) patients who transitioned from PrEP to PIP, and 22 (27.8%) patients who transitioned from PIP to PrEP. No HIV seroconversions were detected during the course of this study.

Conclusion: PIP is helpful HIV prevention modality for individuals with a low frequency of high-risk HIV exposures.

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Introduction

Biomedical prophylaxis against HIV using antiretroviral medications (ARVs) is effective at preventing infection in individuals at greater risk of HIV acquisition, with preexposure prophylaxis (PrEP) and postexposure prophylaxis (PEP) constituting the two major prevention strategies [1,2]. PrEP involves the proactive use of tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) in HIV-negative individuals at risk for HIV infection, and the medication is taken either daily or in an 'on-demand' (also referred to as 'event driven') manner [3]. In contrast, PEP is a retroactive HIV prevention modality where ARVs are initiated within 72 h of a potential HIV exposure and continued for 28 days [1,4].

We previously identified a cohort of individuals experiencing high-risk but infrequent exposures to HIV who were interested in a biomedical HIV prevention modality [5]. For this cohort, daily PrEP would involve greater financial costs and a high pill burden relative to the infrequent exposures. On-demand PrEP may not be appropriate because of many individuals not knowing ahead of time that they were going to be sexually active, and the relative paucity of evidence that this prevention modality would be effective, given the infrequency of exposures [6]. This study evaluates the longer term follow-up of a cohort of individuals using an HIV postexposure prophylaxis-in-pocket ('PIP') strategy for the prevention of low-frequency but high-risk HIV exposures [5].

Methods

This is a retrospective, multicenter analysis of patients using PIP as their primary HIV prevention modality between 1 January 2016 to 31 May 2019, at the Toronto General Hospital (TGH) HIV Prevention Clinic and St. Michael's Hospital (SMH) HIV Clinic, both in Toronto, Canada. TGH is a member of the University Health Network, and the HIV Prevention Clinic receives community referrals and referrals directly from the emergency departments of Toronto General and Toronto Western Hospitals, and Mt. Sinai Hospital.

Participants were referred to the TGH and SMH study sites from emergency departments, primary care providers, and sexual health clinics for consideration of a biomedical HIV prevention strategy. Referred patients were counselled about different HIV prevention modalities, including daily or on-demand PrEP based on their risk factors and in accordance with current guidelines [1,2]. Patients identified to have infrequent HIV exposures (zero to four per year) were also counselled about PIP as a potential HIV prevention modality. Those interested in PIP were counselled that they would be given a prescription for ARVs that included TDF/FTC

300/200 mg daily, with dolutegravir 50 mg daily, both for 28 days. As of November 2018, people of childbearing potential were offered TDF/FTC 300/200 mg with raltegravir 400 mg twice daily, both for 28 days, given the potential association of dolutegravir with neural tube deficits in the developing fetus [7,8]. Patients were counselled to fill the prescription and to have the medication nearby should they have a potential HIV exposure. They were advised to initiate PIP promptly, and no later than 72 h, following a potential HIV exposure. Patients were counselled that potential HIV exposures include condomless vaginal or anal sex with partners whom they were not confident about having a negative HIV status, or with partners that are known to be HIV-positive with a detectable (or possibly detectable) viral load. Additionally, patients were counselled about the sharing of injection drug paraphernalia as a potential HIV exposure. Patients were counselled to complete their 28-day course of ARV in accordance to current PEP guidelines [1,4]. If PIP was initiated, patients were counselled to return to clinic within the first week of starting ARVs for baseline HIV screening and further clinical assessment. Further details of PIP use are available in Appendix 1, <http://links.lww.com/QAD/B587>.

We extracted data retrospectively through a standardized data-collection tool that accounted for demographic data, previous PrEP or PEP use, duration of time using PIP as a primary HIV prevention strategy, occasions of PIP use, and changes between HIV prevention modalities. We entered data into an Excel database (Microsoft Corp., Redmond, WA, USA) and performed descriptive statistics. We compared age and prior PEP usage among participants who initiated PIP versus those who did not. We compared age and prior PEP use as predictors for switching from PrEP to PIP or from PIP to PrEP. Additionally, we evaluated changes from PIP to daily PrEP among patients who used PIP more than once as compared with patients who initiated PIP zero to one time. We used two sample *t*-tests for continuous variables whereas Fisher's exact test and chi-square tests were used for categorical variables, as appropriate.

Results

Between 1 January 2016 through 31 May 2019, 79 patients were prescribed PIP. Baseline demographic characteristics and PIP-use data are highlighted in Table 1. Participants were mainly MSM (75; 94.9%). One person was a woman who injected drugs. The mean age of the participants was 37.5 years (range: 21–70), and mean duration of PIP as a primary HIV preventive strategy was 14.8 months with 1168 patient-months of follow-up (97.3 patient-years). Previous uses of PEP were noted in 32 (40.5%) patients.

Twenty-one (26.6%) patients initiated their PIP medications. There were a total of 32 PIP courses taken by these

Table 1. Baseline characteristics of 79 patients initiated on HIV pre-exposure prophylaxis-in-pocket.

Characteristic	Value
Male sex [<i>n</i> (%)]	75 (94.9%)
Age [mean (range)]	37.5 (21–70)
Months on PIP (mean)	14.8
Cumulative months on PIP	1168
Patients used PIP [<i>n</i> (%)]	21 (26.5%)
PIP courses used (<i>n</i>)	32
Previous PEP use [<i>n</i> (%)]	32 (40.5%)
Transitioned from PIP to PrEP [<i>n</i> (%)]	22 (27.8%)
Transitioned from PrEP to PIP [<i>n</i> (%)]	13 (16.5%)

PEP, postexposure prophylaxis; PIP, pre-exposure prophylaxis-in-pocket; PrEP, pre-exposure prophylaxis.

21 participants, with seven patients using more than one course. All PIP courses were initiated within 72 h of a potential HIV exposure, and all adhered to the 28-day course of PIP, by patient report. Only one patient initiated PIP where clinical staff did not feel ARVs were warranted (condoms were used appropriately) and PIP was discontinued within a week at the subsequent clinic appointment after consultation with the patient. No HIV seroconversions were detected in any of the study participants on subsequent routine testing during the course of this study. Bacterial sexually transmitted infections were detected in five patients (6%) at baseline and in two patients (2.5%) at follow-up appointments. Clinic follow-up rates were 91.1%, with 100% of the 65 patients cared for at the TGH site and 50% of the 14 patients cared for at the SMH site returning to clinic for care.

Among our cohort of 79 participants, 13 (16.5%) patients were initially on PrEP prior to transitioning to PIP, whereas 22 (27.8%) patients initially initiated on PIP (including five of the seven patients who used PIP more than once) transitioned to PrEP because of an increasing frequency of condomless sex. There was no significant difference in age ($38.5 \text{ years} \pm 10.8$) and ($37.1 \text{ years} \pm 10.8$) between those who used their PIP compared with those who did not ($t=0.49$, $P=0.63$). Similarly, prior PEP use was not a significant predictor for initiating PIP ($\chi^2=0.07$, $P=0.79$). There were no statistical differences between those who switched HIV prevention modalities in terms of prior PEP use ($P=1.0$), and age ($t=0.74$, $P=0.46$). Participants who initiated PIP more than once were significantly more likely to switch their HIV prevention modality from PIP to daily PrEP ($P=0.02$).

Discussion

PIP may be a valuable HIV prevention modality for individuals with a low frequency of HIV exposures. Here, we demonstrate the effectiveness of PIP for the

prevention of HIV in a cohort of 79 participants followed over 97.3 patient-years. All PIP use was appropriately initiated within a 72 h window of a potential HIV exposure and no HIV seroconversions occurred throughout our study period.

PIP may offer considerable benefits over routine PEP care for selected individuals. PEP effectiveness has been demonstrated in many observational studies [9,10]; however, patients face many barriers to PEP use, including the recognition that a significant HIV exposure occurred and then presenting to a healthcare facility within 72 h of that exposure. Unfortunately, many patients do not present within that time window and miss an opportunity for HIV prevention [11]. Those that do present to emergency departments and are provided with PEP starter kits have very high attrition rates between the emergency department and clinic, and the attrition rates continue with subsequent follow-up appointments [12,13]. Adherence to conventional PEP models (e.g. when a starter kit is provided in the emergency department, and patients are to be followed up in clinic) is also low, with one study demonstrating only 23.9% of patients completing the 28-day course [13]. A systematic review by Ford *et al.* [14] showed higher completion rates of PEP amongst patients, given a full 28-day course of PEP as opposed to a starter pack. PIP alleviates many of these barriers as patients have immediate access to their full 28-day course of medications and can initiate them should a potential exposure occur without the urgent need to present to a healthcare facility. Although event-driven PEP was attempted in the past, patients were provided only with a 4-day starter kit and asked to present to medical care to receive the remainder of the 28-day course [15]. This study used zidovudine and lamivudine for PEP; however, these readily accessible PEP starter kits were not associated with reduced HIV transmission rates [15]. We opted to provide the entire 28 days of ARV, such that those who may not be adherent to clinic appointments still had the opportunity to complete the 28 days of PEP.

Daily and on-demand PrEP are also effective HIV prevention modalities; however, gaps exist in these proactive approaches, and PIP may be a more viable alternative for carefully selected patients. Daily PrEP has a high pill burden and may be cost-prohibitive for individuals, even with financial support through private or public insurance. Additionally, patients may not want to take a daily tablet for a potential HIV exposure that may occur zero-to-four times per year [16]. On-demand PrEP was designed in part to minimize these downsides; however, on average, the sample studied in the trial reported more than once-weekly exposures, raising uncertainty regarding the effectiveness of this approach for less frequent exposures [3,17]. A substudy of the ANRS IPERGAY trial demonstrated efficacy of on-demand PrEP for those with a lower frequency of sexual

activity, however, individuals were still using a median of 15 tablets of TDF/FTC per month [6], so it is still unclear if on-demand PrEP would be effective with the lower frequency of potential HIV exposures in the patient population described in this study. Additionally, on-demand PrEP requires an individual to start ARVs at least 2 h before a condomless sexual exposure. In our experience, many patients who end up using PIP did not know they were going to be sexually active in advance, or were using condoms that ultimately tore; on-demand PrEP would not have been initiated in a timely manner in such situations.

Patients in our cohort had evolving HIV acquisition risks requiring several changes to their choice of biomedical HIV prevention modality. Patients transitioned between PrEP and PIP based on their exposure frequency, those who used PIP more than once were significantly more likely to transition to daily PrEP. This highlights the need for constant re-evaluation of HIV-acquisition risk with an evaluation and possible change of the HIV prevention modality to meet the current needs of patients.

As highlighted in our previous study, PIP offers several advantages compared with other HIV prevention modalities for carefully selected individuals with very infrequent but high-risk exposures [5]. PIP allows for the prompt initiation of ARVs following a potential HIV exposure, eliminates the need for urgent emergency department visits and subsequent referral to a specialized clinic, gives patients autonomy over their care, and allows for the democratization of ARV access. Additionally, having access to a full 28-day course is associated with greater adherence rates compared with PEP starter packs [14]. PIP requires that patients demonstrate reliability, health literacy, and self-awareness to initiate and adhere to ARVs and to follow-up at subsequent clinic appointments. Limitations of this study include a modest sample size, retrospective design, lack of a control group, and predominance of MSM within our cohort, which may limit the generalizability to other at-risk populations. Prospective studies are underway to further evaluate PIP in clinical practice. Additionally, access to PIP may be an issue because of costs or other locally relevant barriers to healthcare. As infrequent HIV exposures are anticipated (and as there is no immediacy to initiate medications), we found that working closely with our allied health colleagues facilitated access to care by exploring local mechanisms to proactively acquire 28 days of medication.

PIP is a useful HIV prevention strategy for individuals interested in a biomedical HIV prevention modality who have infrequent high-risk exposures to HIV. Given the fluidity in HIV risk over time, regular follow-up with patients may ensure that they are on an HIV prevention strategy tailored to their individual needs.

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Conflicts of interest

There are no conflicts of interest.

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