Outcomes of Individuals Using HIV Postexposure Prophylaxis-In-Pocket ("PIP") for Low-Frequency, High-Risk Exposures in Toronto, Canada

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Background: HIV postexposure prophylaxis-in-pocket ("PIP") is a self-initiated, event-driven HIV prevention modality for individuals with a low frequency of HIV exposures.

Methods: A cohort of 111 patients using PIP as their primary HIV prevention modality was longitudinally evaluated for PIP self-initiation, HIV and sexual transmitted infections, and switching to other HIV prevention modalities between February 2016 and December 2022.

Results: A total of 111 patients had 178.7 cumulative patient-years of PIP use. PIP was self-initiated 69 times by 35 (31.5%) individuals, with 0 HIV seroconversions identified. Thirty four individuals (30.6%) transitioned from PIP to pre-exposure prophylaxis and 33 individuals (29.7%) switched from pre-exposure prophylaxis to PIP.

Conclusions: PIP is a useful addition to other pharmacologic HIV prevention tools, and may help prevent infection in those with a lower frequency of unanticipated HIV exposures.

Key Words: HIV, postexposure prophylaxis, PEP, PEP-in-pocket, PIP, prevention

(*J Acquir Immune Defic Syndr* 2023;94:211–213)

INTRODUCTION

Pre-exposure prophylaxis (PrEP) and postexposure prophylaxis (PEP) are 2 well-established methods to prevent HIV infection through the use of antiretroviral (ARV) medications.[1,2] PrEP is a proactive modality for HIV-negative individuals that typically involves taking a two-drug ARV regimen of tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) daily, or in an "on-demand" (or, "event-driven") manner. In contrast to the proactive nature of PrEP, PEP is a retroactive modality that involves initiating a 28-day course of a three-drug ARV regimen within 72 hours of a potential exposure to HIV.

Significant barriers remain for PrEP and PEP care.[3] For individuals with infrequent and unanticipated higher-risk HIV exposures, the benefits of daily PrEP may be limited beacause of side effects, cost, daily pill burden, or other barriers. Although on-demand PrEP is helpful in reducing cost and pill burden, evidence of efficacy only exists for gay, bisexual, and other men who have sex with men (gbMSM) and its use is limited to circumstances where exposures can be anticipated. Although PEP is highly efficacious,[1] individuals must find and present to an emergency department (ED) or urgent care center that provides PEP within 72 hours of a potential exposure to receive the initial medication dose(s), and an urgent follow-up appointment with a PEP provider for further evaluation and provision of the remaining medications.[1,2] Patient attrition rates between EDs/urgent care centers and follow-up appointments with a PEP provider remain unacceptably high.[3] Additional low-barrier biomedical HIV prevention options would be helpful for individuals who have a low frequency of unanticipated exposures.[3,4]

HIV postexposure prophylaxis-in-pocket ("PEP-in-Pocket" or "PIP") involves prospectively identifying individuals with a very low frequency of higher-risk HIV exposures and providing them with a prescription for 28-days of PEP, along with instructions on when to initiate medications and how to follow-up with care. We previously described PIP care in a cohort of individuals who fit these criteria.[5–7] Here, we present longer-term follow-up and outcomes of this cohort of patients provided with PIP for HIV prevention.

METHODS

We conducted a retrospective evaluation of the clinical characteristics and outcomes of a cohort of patients using PIP for HIV prevention between February 2016 and December 2022 at 2 large HIV-prevention and care centers in Toronto, Canada. Patients were referred to clinical study sites by EDs, primary care providers, and sexual health clinics for consideration of PrEP or PEP. Patients identified as having an anticipated low frequency (0–4 times per year) of higher-risk HIV exposures of any type were provided the option of PIP as a prevention strategy. The HIV prevention method was chosen based on shared decision-making between patients and clinicians and was not protocolized by this study. Those interested in PIP were given a 28-day prescription for a three-drug ARV

Received for publication April 23, 2023; accepted July 5, 2023.

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This work is supported by a grant from the Canadian Institutes of Health Research [Grant number PJT- 175009].

IIB has consulted to BlueDot, a social benefit corporation that tracks emerging infectious diseases, and to the NHL Players' Association.

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regimen, along with instructions on when to initiate medications and how to follow up with care. Typical regimens prescribed included coformulated bictegravir (BIC) 50 mg, emtricitabine 200 mg, and tenofovir alafenamide (TAF) 25 mg (BIC/FTC/TAF) or dolutegravir (DTG) 50 mg plus coformulated TDF 300 mg and emtricitabine 200 mg plus (DTG + TDF/FTC) once daily. Between 2018 and 2021, some people of childbearing potential were prescribed raltegravir 400 mg twice daily in place of dolutegravir, given early reports of its rare, but potential association with neural tube defects in developing fetuses.[8]

Patients were encouraged to fill their prescription and have the medication readily available in an accessible location. Clinic social workers provided support in accessing government assistance programs to those without prescription drug coverage. Patients were counselled to self-initiate PIP as soon as possible and within a 72-hour window after a potential HIV exposure, which included condomless vaginal or anal sex with a partner of unknown HIV status or known to be HIV-positive with a potentially detectable viral load and/or the nonsterile use of any injection drug equipment. Patients were also counselled to complete their 28-day course of ARVs in accordance with current PEP guidelines,[1,2] and to present to the clinic on a nonurgent basis within the first week of initiating ARVs for baseline HIV and sexually transmitted infection (STI) screening (including urine, pharyngeal, and rectal screening for chlamydia and gonorrhea, and syphilis testing), and routine safety laboratory investigations.

Participants were seen in clinics at regular 5–6 month intervals, or sooner if PIP was self-initiated. At follow-up clinic visits, patients were screened for HIV, hepatitis C, and bacterial STIs. Patients were also asked about PIP use in the previous months and their current and projected HIV risk to determine whether a change in HIV prevention modality was warranted (eg, transition from PIP to PrEP). In addition, patients were screened for mental health or substance abuse issues and connected to care where appropriate. Data were extracted retrospectively using a standardized form that included basic demographic information, instances of PIP use, cumulative duration on PIP, adherence to PIP, transitions between HIV prevention modalities (ie, PIP-to-PrEP or PrEP-to-PIP), results from HIV and STI testing performed at study sites, and self-reported STIs. Data were entered into a Microsoft Excel database (Redmond, WA) and descriptive statistics were performed. Some participants included were also enrolled in a prospective study evaluating PIP acceptability and adherence.

RESULTS

PIP was prescribed to 111 individuals between February 2016 and December 2022, giving a combined total of 178.7 patient-years. The average age was 36.6 years old (range 18–69), with 106 (95.5%) patients assigned male sex at birth. Thirty-five (31.5%) patients self-initiated their prescribed PIP, and a total of 69 courses of PIP were completed during the observed time. Based on self-reported data, all 69 episodes were initiated for condomless sex; none were initiated for injection drug use. The most common regimens used were DTG + TDF/FTC (n = 51), followed by BIC/TAF/FTC (n = 6), and raltegravir + TDF/FTC (n = 2).

HIV and STI screening were completed within 6 months of PIP initiation for 98.6% (68/69) of the reported instances. Medications were discontinued on 5 occasions; 4 times (5.8%) by PIP-providers recommending discontinuing medications after a risk evaluation, and there was 1 instance (1.4%) of self-discontinuation because of medication side effects. There were no HIV seroconversions.

In 90 individuals for whom there are data, there were 22 self-reported or laboratory-detected episodes of bacterial STIs in 13 individuals (14.4%) using PIP; rectal chlamydia (n = 9), urethral chlamydia (n = 1), rectal gonorrhea (n = 4), urethral gonorrhea (n = 1), and pharyngeal gonorrhea (n = 7).

Patients fluidly transitioned between HIV prevention modalities as circumstances warranted: 34 individuals (30.6%) changed from PIP to PrEP and 33 individuals (29.7%) shifted from PrEP to PIP. Of the 34 who switched from PIP to PrEP, 15 had never self-initiated PIP, 9 had self-initiated PIP once, and 10 had self-initiated PIP 2 or more times. Although reasons for switching were not formally collected, motives were most frequently reported as changes in relationship status and/or the number of current or anticipated sexual partners.

DISCUSSION

PIP is an effective HIV prevention modality for people with a low frequency of higher-risk HIV exposures that are often (but not always) unanticipated, who are interested in biomedical prevention strategies. Our data demonstrate the utility of PIP for HIV prevention in a cohort of 111 patients, with a combined total of 178.7 patient-years of PIP use, and the ability to seamlessly transition between PIP and PrEP based on shared decision-making between patients and their providers.

Significant barriers to PEP remain.[3,4] PEP requires an individual to present to an ED or urgent care facility in a timely manner, at which time they may receive a "starter pack" containing only a few days of ARVs along with a referral to a dedicated PEP provider who will provide further care and determine whether the remainder of ARVs is needed. Those who require a full 28-day course of medication may then face additional challenges because ARVs are expensive and not universally covered for PEP in many jurisdictions, including Ontario. These barriers to care lead to significant attrition, many of which can be mitigated by PIP.[3,9,10]

PIP may be an appropriate alternative to daily or on-demand PrEP for some individuals. For example, individuals with very infrequent (eg, 0–4) exposures per year may weigh costs, side effects, tolerability, and toxicity in favor of PIP rather than daily PrEP[11] and still maintain autonomy over their HIV prevention care. On-demand PrEP requires 2–24 hours of foresight to initiate medications before a potential exposure, which is not always possible in situations of condoms breaking, sexual assault, some injection drug exposures, or more spontaneous sexual encounters. Importantly, current data demonstrate efficacy for infrequent on-demand PrEP when used 2–3 times per month in gbMSM

only.[12] It is not entirely clear what degree of protection on-demand PrEP affords women or individuals who use it even less frequently, and this is not recommended for use in these scenarios.[11]

PIP facilitates health care engagement for people at risk for HIV with routine HIV and STI testing every 5–6 months; some individuals using PIP do not want to use PrEP, and may not otherwise be seen by a health care professional on a routine basis.[5,6] Prospectively identifying individuals who are appropriate candidates for PIP and providing them with a full 28-day prescription and education on when to self-initiate medications provides people with autonomy and agency over their HIV prevention care, the possibility for shorter times between HIV exposures and initiating ARVs, and enables timely access to ARVs without the urgent need to seek health care.[5,6,13,14] PIP's proactive identification of individuals who may require PEP allows for nonurgent referral to social workers or community partners who can help navigate financial assistance to obtain ARVs for those in need.

There are several limitations to this study. The participants were predominantly gbMSM, and further studies are needed to ascertain whether PIP is beneficial for other populations, including women, sex workers and people who inject drugs. Furthermore, this work was conducted at 2 major hospital-based clinics in Toronto, Canada, and therefore experiences may not be generalizable to other practice settings or regions. Data were collected retrospectively, such that we cannot report on the frequency of missed opportunities for PIP use. In addition, laboratory test results for HIV/STIs were not available for all participants and patients may have sought testing outside of study sites. We did not include a control group, and hence cannot comment on how patient outcomes may have differed with alternative HIV prevention strategies such as daily or on-demand PrEP. Prospective studies are currently evaluating PIP versus other HIV prevention modalities for individuals at similar low risk for HIV acquisition.

We envision PIP being a useful prevention strategy for individuals with infrequent HIV exposures who cannot or do not want to take daily PrEP, where on-demand PrEP may not be feasible or advised, or who face barriers accessing PEP, and who want autonomy and agency over their care. Qualitative studies are underway that assess the attitudes, beliefs, and acceptability of PIP. PIP is an innovative and useful HIV prevention modality for individuals with a low frequency of higher-risk HIV exposures.

REFERENCES

1. Tan DHS, Hull MW, Yoong D, et al. Canadian guideline on HIV pre-exposure prophylaxis and nonoccupational postexposure prophylaxis. *Can Med Assoc J.* 2017;189:E1448–E1458.
2. Centers for Disease Control and Prevention: US Public Health Service. Preexposure prophylaxis for the prevention of HIV infection in the United States—2021 Update: a clinical practice guideline. Available at: https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prepguidelines-2021.pdf; 2021. Accessed July 4, 2023.
3. Bogoch II, Scully EP, Zachary KC, et al. Patient attrition between the emergency department and clinic among individuals presenting for HIV nonoccupational postexposure prophylaxis. *Clin Infect Dis.* 2014;58:1618–1624.
4. Amato AT, Kiffer C, Ben K, et al. Barriers to PrEP uptake in two spirit, gay, bisexual, trans and queer men, and non-binary people in Canada: an analysis considering indigeneity, ethnoracial and gender-diverse identities within a community-based health survey. ScienceOpen Posters. January 24, 2024. Available at: https://www.cbrc.net/barriers_to_prep_uptake. Accessed July 1, 2023.
5. Tumarkin E, Heendeniya A, Murphy P, et al. Brief report: HIV postexposure prophylaxis-in-pocket ("PIP") for individuals with low-frequency, high-risk HIV exposures. *J Acquir Immune Defic Syndr.* 2018;78:20–22.
6. Alghamdi A, Hempel A, Heendeniya A, et al. HIV postexposure prophylaxis-in-pocket: long-term follow-up of individuals with low-frequency, high-risk HIV exposures. *AIDS.* 2020;34:433–437.
7. Heendeniya A, Bogoch II. HIV prevention with post-exposure prophylaxis-in-pocket. *Lancet Public Health.* 2019;4:e494.
8. Zash R, Makhema J, Shapiro RL. Neural-tube defects with dolutegravir treatment from the time of conception. *N Engl J Med.* 2018;379:979–981.
9. Inciarte A, Leal L, Masfarre L, et al. Post-exposure prophylaxis for HIV infection in sexual assault victims. *HIV Med.* 2020;21:43–52.
10. Chacko L, Ford N, Sbaiti M, et al. Adherence to HIV post-exposure prophylaxis in victims of sexual assault: a systematic review and meta-analysis. *Sex Transm Infect.* 2012;88:335–341.
11. Molina JM, Capitant C, Spire B, et al. On-demand preexposure prophylaxis in men at high risk for HIV-1 infection. *N Engl J Med.* 2015;373:2237–2246.
12. Molina JM, Charreau I, Spire B, et al. Efficacy, safety, and effect on sexual behaviour of on-demand pre-exposure prophylaxis for HIV in men who have sex with men: an observational cohort study. *Lancet HIV.* 2017;4:e402–e410.
13. Ford N, Venter F, Irvine C, et al. Starter packs versus full prescription of antiretroviral drugs for postexposure prophylaxis: a systematic review. *Clin Infect Dis.* 2015;60(suppl 3):S182–S186.
14. Fox JM, Lee MJ, Fairhead CL, et al. Self-start HIV postexposure prophylaxis (PEPSE), to reduce time to first dose and increase efficacy. *Sex Transm Infect.* 2022;0:1–2022-055622.