Research Article
Volume 15:1, 2025

Journal of Blood & Lymph

ISSN: :2165-7831 Open Access

Low Adherence to Post-Exposure Prophylaxis Follow-Up, When Less Can Be More

Elaine Monteiro Matsuda[1*] and Luis Fernando de Macedo Brigido[2]

[1]*Department of Health Sciences, Santo André Health Secretary, Sao Paulo, Santo Andre, Sao Paulo, Brazil*

[2]*Department of Virology, Virology Center, Adolfo Lutz Institute, Sao Paulo, Sao Paulo, Brazil*

Abstract

Although Post-Exposure Prophylaxis (PEP) is a powerful tool to abort HIV infection within 72 hours of exposure, blocking the establishment of chronic infection, follow-up metrics of this intervention are scarce. As antiretroviral use delays diagnosis biomarkers, so the moment to perform serological evaluations must consider this to avoid missing diagnosis. We assessed the adherence to follow up visits after PEP dispensation in a service in the Sao Paulo metropolitan area and reviewed the literature, both showing limited adherence to current protocols, leading to difficulties of diagnose early HIV infection. The current proposed date for the first return after PEP is both associated with low adherence and if infection has occurred, too early to detect antibodies in some patients. Guidelines should allow or promote a longer time for follow up visits after PEP discontinuation along with continued contact as with message reminders maximizing the benefit for both patient and community.

Keywords: Post-Exposure Prophylaxis (PEP) • HIV infection • Community

Introduction

Antiretrovirals can provide not only treatment but also act as a preventive intervention through viral suppression (undetectable=untransmissible) effective as Pre-Exposure (PrEP) and Post-Exposure Prophylaxis (PEP). The preferred regimen to the first line treatment in Brazil, is the same used for PEP and consists of tenofovir 300 mg/lamivudine 300mg associated with dolutegravir 50 mg (TDF/3TC+DTG) daily, prescribed after a point-of-care serological HIV test and dispensed for 28 days with guidance to repeat the HIV test. The timing of this follow-up testing varies between four to six weeks and 12 weeks after exposure. The CDC (USA) and the UK recommend the use of a fourth generation test at the beginning of PEP and if not used, the CDC recommends an additional serological follow up 6 months after exposure [1-9].

Moreover, early/primary HIV infection already established at the time of PEP initiation is a possibility in many situations. Fourth-generation rapid test is more efficient in detecting very recent infections, due both to the occasional detection of the p24 antigen in acute infection as well as improving antibodies detection, missed by some third-generation rapid tests.

To evaluate adherence to post-exposure prophylaxis follow-up, we carried out this study in a reference service that cares for people living with HIV and provides antiretroviral prophylaxis in Santo Andre, a metropolitan area of Sao Paulo/Brazil.

Materials and Methods

The Medication Logistics Control System (SICLOM) provided information on users with PEP dispensation between 2019-2021. Medical records were consulted to assess adherence to the recommended 30 and 120-day returns after risk exposure and other variables. Return after starting PEP between 26 and 40 days was considered for this study as a 30-day return, between 110 and 130 days as a 120-day return intermediary it was between 41 and 109 days. Return on any date within 180 days was also evaluated. Data were anonymized and the statistical analyzes were performed with Stata version 14.2 (Stata Corp LLC, College Station, Texas, USA).

During the study period, we obtained 2168 PEP events recorded at SICLOM, dispensed for 1468 users. Additional information could be obtained from 1281/1468 users. The median age of these users was 31 years old (IQR25-75 24-39), with 6/1281 0.3% being under 14 years

***Address for Correspondence:** Elaine Monteiro Matsuda, Santo Andre Health Secretary, Sao Paulo, Santo Andre, São Paulo, Brazil. E-mail: lubrigido@gmail.com*

Received: 26 April, 2024, Manuscript No. JBL-24-133202; **Editor assigned:** 30 April, 2024, PreQC No. JBL-24-133202 (PQ); **Reviewed:** 14 May, 2024, QC No. JBL-24-133202; **Revised:** 06 May, 2025, Manuscript No. JBL-24-133202 (R); **Published:** 13 May, 2025, DOI: 10.37421/ 2165-7831.2025.15.343

and 17/1281 0.8% being above 60 years. Most were male (853/1281 67%), with 368/853 43% of this reporting being men who have sex with men (MSM), 39/853 4.6% identified as Transgender Women (TW), which corresponds to 27/931 2.9% among all users. Almost all TW were sex workers, 90% 35/39 versus 2.4%29/1207 among ciswomen (p<0.0001). Among cisgender, the proportion of sex worker's women was higher than among men, 5.4% 23/428 versus 0.7% 6/808 (p<0.0001).

Results and Discussion

We verified a change in the profile of PEP users who sought the service, still young adults, but with increasing age, with a median of 30, 31 and 32 years old, in 2019, 2020 and 2021, respectively (p=0.02) and a proportional increase of women 31%, 28% and 51% (p<0.0001), which may be related in part to the increase of occupational accidents during the study period 27%, 33% and 53%, mostly women 70%, 74%, 76%.

Table 1 demonstrates adherence to returns defined as 30-day, intermediary, 120-day any time up to 180 days. There was a reduction in PEP follow-up during the COVID-19 pandemic, with adherence better in the 30-day than 120-day return, 315/1281 (24,6%) versus 103/1281 (8%, p<0.0001).

Table 1. Adherence to the returns of 30-day (26-40), 120-day (110-130) and intermediate (41-109) or at any time within 180 days after post-exposure prophylaxis

Adherence		ALL	2019	2020	2021	p
30-day return	Yes	315 24.6%	230 36.3%	45 10.7%	38 17%	0.0001
	No	966 75.4%	404 63.7%	377 54.7%	185 83%	
Intermediary return median of 57 days (IQR25-75 43-67)	Yes	79 6.2%	60 9.4%	9 2.1%	10 4.5%	0.12
	No	1202 93.8%	576 90.6%	413 97.9%	213 95.5%	
120-day return	Yes	103 8%	77 12.2%	13 3.1%	12 5.4%	0.03
	No	1178 92%	557 87.8%	409 96.9%	211 94.6%	
Return at any time	Yes	350 27.3%	251 39.5%	54 12.8%	45 20.2%	<0.001
	No	931 72.7%	385 60.5%	368 87.3%	178 79.8%	

As the PEP regimen is the same as first line treatment in Brazil, when the HIV infection is not blocked by PEP (viral infection is established), similar to starting PEP in a patient during the acute/early phase, early therapy is instituted. Very early treatment has been suggested to have potential benefits to the patient and surely avoids further viral transmission characteristics of this highly infectious phase. However, recognition of infection is cumbersome at this stage and several studies demonstrate delays in seroconversion and HIV viremia detection due to suppression of antiretroviral drugs, thus decreasing the sensitivity of serology and other biomarkers of infection. False-negative results may either promote further transmission to the community. Delayed initiation of PEP, poor/non-adherence to the regimen, especially in the first days further high-risk sexual exposures after cessation of PEP may compromise the outcome.

Ruling out acute HIV infection before prophylactic antiretroviral use is particularly challenging in low and middle-income settings, where there is limited access to advanced laboratory testing and infrastructure. This issue may be illustrated by the observations of Manak et al. that evaluated the performance of HIV antigen/antibody combination at weeks 12 and 24 following the initiation of antiretroviral therapy at Fiebig stage I (FI), FII or FIII/IV in comparison to samples from untreated cases, who demonstrated robust reactivity, while 52% of samples from individuals initiating ART at FI, 7.7% at FII 4.5% at FIII/IV were nonreactive by the HIV Ag/Ab Combo assays. Although this first evaluation in the use of antiretroviral was at 12 weeks, it would be expected that there would also be a delay with 4 weeks of the use of PEP or PrEP.

Poor follow-up testing also was verified in an Australian cohort of mainly MSM, in which only 34% of 1864 had returned to test at 12 weeks after initiation of PEP, similar to rates reported in the UK (30%-67%). In our study, the first year of the COVID-19 pandemic, assistance to PEP cases was slightly lower compared to 2019 (-4%), with a 10% decrease in 2021 compared to 2020.

Conclusion

The recommended follow-up routine testing was 30 and 120 days after starting PEP. However, in 2020, with the limitations imposed by the COVID-19 pandemic, a self-test was requested to be carried out in 30 days and a return to the service only in 120 days. Despite this guidance, the 30-day return shows a greater adherence than the 120-day return. Even before the pandemic, we found that adherence to the 120-day return (12.2%) was very low and worse than in other studies, perhaps because this return was only suggested at the 30 days' return, even in cases were 120 days' return was emphasized, as at a 30-day visit with negative tests, many patients feel that the 30-day evaluation is sufficient, disregarding further follow-up [10-12].

Because of these issues, in 2023 we started to orient the first return within 45 days after the start of the PEP (the current limit for the first return according to the Brazilian guideline), an attempt to make an earlier diagnosis but providing more time to seroconversion, as 15 days after the interruption of PEP. The UK guideline seems more coherent to this view; it waits at a minimum of 45 days after completion

of the PEP course. If the 28-day PEP course is completed, this is 73 days (10.5 weeks) post-exposure.

Funding Statement

The study was supported in part by grants National council for scientific and technological development (CNPq/MS-DIAHV N° 24/2019-442776/2019-5) and Sao Paulo research foundation (FAPESP/PDIP-PPP2018/14384-9).

Ethical Committee

This study was approved by Institutional ethical committee (Faculty of Medicine of ABC, CAAE: 21164819.7.0000.0082).

Author Contributions

Conceptualization, formal analysis, data curation and manuscript were writing original draft by Elaine Monteiro Matsuda. The funding acquisition and writing-review and editing were carried out by Louis Fernando of Macedo Brigido.

Conclusion

The PEP return protocol in 30 and 120 days has low adherence on all dates. This is aggravated by the fact that adherence is greater on the first (day-30), close to the end of the PEP, which may increase the chances of false negative results. Also, the return in 120 days seems very far from the event the user may not return. We strongly suggest incorporating some recommendations from the UK Guideline, which services use text/email reminders, to encourage adherence to post-exposure HIV testing. Studies are needed to define a better time to associate adherence and the test's ability to detect seroconversion. Moreover, strategies to identify infections in those infected before or during PEP are needed to avoid ART discontinuation, as these cases of very early treatment could favor future control strategies.

References

1. Stone, Louise. "The Perfect Partner: No Hiv Transmission with Art." *Nat Rev Urol* 16 (2019): 387-387.
2. Gokengin, Deniz, Dominik Bursa, Agata Skrzat-Klapaczynska Ivailo Alexiev, Elena Arsikj, et al. "Prep Scale-Up and PEP in Central and Eastern Europe: Changes in Time and the Challenges We Face with No Expected HIV Vaccine in the Near Future." *Vaccines* 11 (2023): 122.
3. Virais, Hepatites. "Protocolo Clínico E Diretrizes Terapêuticas Para Profilaxia Pós-Exposição De Risco (Pep) À Infecção Pelo Hiv, Ist E."
4. Wang, Yao, Shaochu Liu, Yan Zhang Wei Tan, et al. "Use of HIV Post-Exposure Prophylaxis among Men Who have Sex with Men in Shenzhen, China: A Serial Cross-Sectional Study." *AIDS Behav* 26 (2022): 3231-3241.
5. Cresswell, Fiona, Kaveh Asanati, Sanjay Bhagani Marta Boffito, et al. "UK Guideline for the Use of HIV Post-Exposure Prophylaxis 2021." *HIV Med* 23 (2022): 494-545.
6. Ambrosioni, Juan, Laura Levi, Jasmini Alagaratnam Kathrin Van Bremen, et al. "Major Revision Version 12.0 of the European AIDS Clinical Society Guidelines 2023." *HIV Med* 24 (2023): 1126-1136.
7. Guidelines on Post-Exposure Prophylaxis for HIV and the Use of Co-Trimoxazole Prophylaxis for HIV-Related Infections Among Adults, Adolescents and Children: Recommendations for a Public Health Approach. *WHO* 2014.
8. Matsuda, Elaine Monteiro, Cintia Mayumi Ahagon, Luana Portes Ozório Coelho Ivana Barros Campos, et al. "A Simple Algorithm for Selecting Cases to Investigate Acute and Early HIV Infections in Low-and Middle-Income Countries." *J Med Virol* 94 (2022): 791-794.
9. Elliott, Tamara, Eduard J. Sanders, Meg Doherty Thumbi Ndung'u, et al. "Challenges of HIV Diagnosis and Management in the Context of Pre-Exposure Prophylaxis (Prep), Post-Exposure Prophylaxis (PEP), Test and Start and Acute HIV Infection: A Scoping Review." *J Int AIDS Soc* 22 (2019).
10. Manak, Mark M, Linda L. Jagodzinski, Ashley Shutt Jennifer A. Malia, et al. "Decreased Seroreactivity in Individuals Initiating Antiretroviral Therapy During Acute HIV Infection." *J Clin Microbiol* 57 (2019): 10-1128.
11. Armishaw, Judy, JF Hoy, KM Watson EJ Wright, BG Price, et al. "Non-occupational Post-exposure Prophylaxis in Victoria, Australia: Responding to High Rates of Re-presentation and Low Rates of Follow-up." *Int J STD AIDS* 22 (2011): 714-718.
12. Matsuda, Elaine Monteiro, Isabela Penteriche de Oliveira Laura Ballesteros Bao, et al. "Impact of COVID-19 on People Living with HIV-1: Care and Prevention Indicators at a Local and Nationwide level, Santo André, Brazil." *Rev Saude Publica* 56 (2022): 37.

How to cite this article: Matsuda, Elaine Monteiro, and Luis Fernando de Macedo Brigido. "Low Adherence to Post-Exposure Prophylaxis Follow-Up, When Less Can Be More." *J Blood Lymph* 15 (2025): 343.